EXHIBIT 1

Exhibit A-01

"Nitric oxide synthase and nitric oxide-mediated effects in lower urinary tract smooth muscles"

("Andersson")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Andersson teaches a method for prophylaxis or treatment of benign prostatic hyperplasia. Andersson discloses a potential pathway to smooth muscle relaxation of the urogenital system for the treatment of micturition as well as unstable bladder conditions, both of which are symptomatic of benign prostatic hyperplasia. (274, 277, 278) The reference teaches that "nerve-induced relaxation of the rabbit urethra increases the smooth-muscle content of cGMP but not cAMP. Inhibition of NOS by N^C-nitro-L-arginine prevented both the urethral relaxation and the increase in cGMP content. Furthermore, in the presence of the cGMP-phosphodiesterase inhibitor Zaprinast, the increase in cGMP levels was more pronounced. Thus, it seems that cGMP has a role as a second messenger in the rabbit urethra and that this system is activated during NANC nerve-mediated relaxation." Andersson teaches that "[a]n inhibitory, relaxation-mediating system may serve not only the detrusor, the trigone, and the bladder neck/urethra, but may also be of importance for their integrated function." (274) Thus, Andersson teaches the benefit of use of a PDE V inhibitor, here Zaprinast, to increase cGMP concentration to enhance smooth muscle relaxation in connection with treatment of symptoms associated with BPH, including bladder instability.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound	Andersson reports on the impact of Zaprinast, a known PDE V inhibitor, as a smooth muscle relaxant in the urogenital system

[1] Andersson, K-E., and Katarina Persson. "Nitric oxide synthase and nitric oxide-mediated effects in lower urinary tract smooth muscles." World journal of urology 12.5 (1994): 274-280. ("Andersson") was published in October 1994.

Claim No.	Claim Language	Description
	selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	and the potential therapeutic pathway for treating micturition and other BPH systems using this pathway. (278) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Andersson discloses zaprinast, a PDE V inhibitor, which can be administered with a pharmacologically acceptable excipient

Claim No.	Claim Language	Description
		(which can include water) in unit dose form. Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. *See, e.g., The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995).*

Exhibit A-02

"Use of quinolones in treatment of prostatitis and lower urinary tract infections"

("Andriole")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Andriole discloses a method for treatment of prostatitis, which is inclusive of BPH.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Andriole discloses the use of quinolones in the treatment of prostatitis. It has been demonstrated that a quinolone known as pyrroloquinolone is an inhibitor of PDE V. *See* W. Jiang, et al., "Pyrroloquinolone PDE5 inhibitors with improved pharmaceutical profiles for clinical studies on erectile dysfunction", J. Med. Chem. 2005, 498, 2126-2133; *see also* Zhihua Sui et al., "Pyriminidinylpyrroloquinolones as highly potent and selective PDE5 inhibitors for treatment of erectile dysfunction," J. Med. Chem. 2002, 45, 4094-4096. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the

[1] Andriole VT, Use of quinolones in treatment of prostatitis and lower urinary tract infections, Eur J Clin Microbiol Infect Dis. 1991 April; 10(4):342-50. ("Andriole") was published in April 1991.

Claim No.	Claim Language	Description
		invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Andriole discloses clinical studies using quinolones in combination with pharmacologically acceptable excipients administered in unit dose form. Moreover, the use of inhibitor compounds in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. *See, e.g., The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995).*

Exhibit A-03

"In vitro profile of UK-92,480, an inhibitor of cyclic GMP-specific phosphodiesterase 5 for the treatment of male erectile dysfunction"

("Ballard")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Ballard does not explicitly disclose a method for treating BPH. However, Ballard discloses that the NO/cGMP system is the main pathway for smooth muscle relaxation in the penis, mediating erection, and that this pathway may have clinical benefit for the prevention and treatment of erectile dysfunction ("ED"). (Abstract 1462) One of ordinary skill in the art would have known that the therapeutic target of smooth muscle relaxation in the penis for treatment of ED was similar to the therapeutic target of relaxation in the prostatic smooth muscle and related lower urinary tract smooth muscle.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole,	Ballard discloses administering a PDE V inhibitor to a person. Ballard teaches that PDE V is present in the smooth muscle tissue of the corpus cavernosum of the penis as confirmed with the use of Zaprinast, a known selective PDE V inhibitor, and that inhibition of PDE V results in relaxation of the penile smooth muscle tissue. (Abstract 1462) Ballard further teaches that "UK-92,480," Sildenafil, is a "potent" selective PDE V inhibitor, which also amplifies the NO/cGMP pathway involved in the relaxation of the corpus cavernosum, results in relaxation of the penile smooth muscle tissue, and may be used in the treatment of ED. (Abstract 1462) Based upon the teachings of this reference, other references

[1] Ballard, S. A., et al. "In vitro profile of UK-92,480, an inhibitor of cyclic GMP-specific phosphodiesterase 5 for the treatment of male erectile dysfunction." J. Urol 155 (1996), Abstract 1462, Proceedings of the American Urological Association, Vol. 155, May 1996 Supplement. ("Ballard") was published in May 1996.

Claim No.	Claim Language	Description
	• 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Ballard discloses and reports on the clinical evaluation of sildenafil, a PDE V inhibitor, administered with a pharmacologically acceptable excipient (which can include water) in unit dose form. Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within

Claim No.	Claim Language	Description
		the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-04

"Relaxant influence of phosphodiesterase inhibitors in the cat gastric fundus"

("Barbier")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Barbier discloses that inhibiters of functionally present PDEs cause relaxation in smooth muscle tissue by increasing the amount of cAMP and/or cGMP. (*See*, *e.g.* Abstract; p. 41-42.) Relaxing smooth muscle is a known therapeutic goal of medications to treat BPH.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-	Barbier discloses administering a PDE V inhibitor to induce smooth muscle relaxation for therapeutic benefit. Barbier teaches that inhibiters of PDE V (including specifically, PDE V inhibitor Zapranist) cause smooth muscle relaxation because of the role of PDE V and NO in the metabolism of cGMP. (*See*, *e.g.* Table 3 and pp. 46-47) If PDE V is present in smooth muscle tissue, use of a PDE V inhibitor will increase cGMP concentration levels and relax the tissue. Thus, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the

[1] Barbier, Ann J., and Romain A. Lefebvre. "Relaxant influence of phosphodiesterase inhibitors in the cat gastric fundus." European journal of pharmacology 276.1 (1995): 41-47. ("Barbier") was published on March 24, 1995.

Barbier

Claim No.	Claim Language	Description
	2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Barbier discloses PDE V inhibitors in combination with pharmacologically acceptable excipients and administered in unit dose form. (p. 42, "2.3 Drugs and materials") Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-05

"Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction"

("Boolell")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Boolell discloses a method for the "effective oral treatment for penile erectile dysfunction."
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Boolell discloses the use of Sildenafil, a selective PDE V inhibitor, as an "oral agent" for the treatment of erectile dysfunction. Sildenafil's effectiveness is tied to the presence of cGMP specific PDEs located in the corpus cavernosum smooth muscle tissue of the penis. Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of

[1]Boolell, Mitradev, et al. "Sildenafil: an orally active type 5 cyclic GMP-specific phosphodiesterase inhibitor for the treatment of penile erectile dysfunction." International journal of impotence research 8.2 (June 1996): 47-52. ("Boolell") was published in June 1996.

Claim No.	Claim Language	Description
		PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Boolell reports on the clinical study of 12 patients who were administered sildenafil, which inherently discloses a PDE V inhibitor in combination with a pharmacologically acceptable excipient administered in a unit dose form. Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-06

"Sildenafil, a novel effective oral therapy for male erectile dysfunction"

("Boolell 2")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Boolell 2 discloses a method for the treatment of erectile dysfunction. (*See, e.g.*, 257, 261.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Boolell 2 discloses the oral administration of an effective amount of sildenafil, an inhibitor of PDE V, to a person in need of treatment for erectile dysfunction. Boolell 2 teaches that the mechanism of penile relaxation involves relaxation of the corpus cavernosal smooth muscle cells mediated by NANC and cholinergic mechanisms – caused by NO and its 2nd messenger cGMP. Use of sildenafil "a potent and competitive inhibitor of PDE V – a cGMP specific enzyme and the predominant enzyme in the corpus cavernosum" is a stated reason for the effectiveness of the treatment. (*See, e.g.* 257, 261.) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention.

[1] Boolell, M., et al. "Sildenafil, a novel effective oral therapy for male erectile dysfunction." British journal of urology 78.2 (August 1996): 257-261. ("Boolell 2") was published in August 1996.

Claim No.	Claim Language	Description
		There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Boolell 2 discloses the oral administration of sildenafil, an inhibitor of PDE V, in combination with a pharmacologically acceptable excipient in unit dose form. (p. 258) Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See*, *e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-07

"Characterization and localization of nitric oxide synthase in the human prostate"

("Burnett")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Burnett discloses methods for the prophylaxis or treatment of BPH. Burnett teaches that "[p]harmacological manipulation of NO in the prostate may… represent an alternative management approach to BPH." (*See* p. 438.) Burnett discloses the existence of nitric oxide synthase ("NOS") activity in the human prostate (similar to other genitourinary organs) and its location in nerves coursing throughout the smooth muscle of the stroma. The presence of NOS implicates nitric oxide ("NO") as a modulator of smooth muscle relaxation in the prostate (as it does in other genitourinary organs). (*See*, p. 435-436, 438.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole,	Burnett teaches that "clinical BPH, which is often related to intrinsic prostatic smooth muscular tone, could be partly explained by a dimunition in NO and its known effects on smooth muscle relaxation. Pharmacologic manipulation of NO in the prostate may, therefore, represent an alternative management approach to BPH." (p. 438) One of ordinary skill in the art, therefore, would be motivated to identify and use known mechanism or agents for pharmacological manipulation of NO in the prostate in order to induce prostatic smooth muscle treat relaxation for the treatment of BPH. Thus, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to

[1] Burnett, Arthur L., et al. "Characterization and localization of nitric oxide synthase in the human prostate." Urology 45.3 (1995): 435-43. ("Burnett") was published on March 1, 1995.

Claim No.	Claim Language	Description
	• 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of PDE V inhibitor in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-08

"Nitric oxide control of lower genitourinary tract functions: a review"

("Burnett 2")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Burnett 2 discloses methods for prophylaxis or treatment of BPH. Burnett 2 teaches the manipulation of nitric oxide ("NO") to elicit relaxant effects in the prostate as a method to treat benign prostatic hyperplasia. (*See,e.g.* pp. 1071-1073; p. 1077 "[i]t is conceivable that NO can be pharmacologically manipulated in this organ [the prostate] . . . to achieve therapeutic objectives").
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one,	Burnett 2 teaches the nitric oxide ("NO") pathway, including the ability of NO to induce guanylate cyclase activity, increase cGMP levels, and relax the smooth muscle tissues in the lower genitourinary system, including the prostate. Table 1 illustrates smooth muscle relaxation that occurs in the presence of NO in the penis, urethra, bladder, male excurrent duct system, and prostate. Burnett 2 then teaches that "[c]linically, NO-based mechanisms may be important for the preservation of normal micturition and urinary continence." (*See, e.g.* pp. 1071-1073; Figure 1; Table 2; p. 1077-1078.) One of ordinary skill in the art would know that relationship between NO and inhibition of PDE V and, therefore, would be motivated and taught to use PDE V inhibitors to relax prostatic smooth muscle to treat BPH. As disclosed by Burnett: "Intense investigations of [nitric oxide] have extended its importance to several genitourinary functions. Penile erection, micturition, peristalsis of the male excurrent duct system, contractile properties of the prostate, and lumbosacral spinal cord neurotransmission are all function that may transpire

[1] Burnett, Arthur L. "Nitric oxide control of lower genitourinary tract functions: a review." Urology 45.6 (June 1995): 1071-1083 ("Burnett 2"). ("Burnett 2") was published in June 1995.

Claim No.	Claim Language	Description
	• 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	under some degree of control of nitric oxide. Impotence, urinary obstruction, or ejaculatory problems, in turn, may represent alterations of nitric oxide production or action. The strategic manipulation of nitric oxide or its mechanism of action, possibly by pharmacological means, may restore or produce desired functional effects." (p. 1078) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed

Claim No.	Claim Language	Description
		invention of the ‘124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of a PDE V inhibitor in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-09

("Caffeine")
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Caffeine, a component of such foods as coffee, chocolate, and various teas, has been consumed for centuries. Caffeine is used in a method for the prophylaxis and treatment of benign prostatic hyperplasia. (*See, e.g.*, E.P. Patent Application Publication 1 020 190 - "Treatment of BPH with cGMP elevators" to Wyllie, published: July 19, 2000 ("Wyllie '190") at [0004] and *generally*.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	The method teaches the administration of an effective amount of caffeine, which include as an active ingredient a PDE V inhibitor, to a person in need thereof. (*See, e.g.* Wyllie '190 at [0004] and *generally*; several publications teach that caffeine is a PDE V inhibitor, including, Beavo, Joseph A. "Cyclic nucleotide phosphodiesterases: functional implications of multiple isoforms." Physiological reviews 75.4 (1995): 725-748 ("Beavo 2") at p. 726, Francis, Sharron H., et al. "Inhibition of cyclic nucleotide phosphodiesterases by methylxanthines and related compounds." Methylxanthines. Springer Berlin Heidelberg, 2011. 93-133 ("Francis") at p. 10 and *generally*, Hendrix, Martin, and Christopher Kallus. "Phosphodiesterase inhibitors: A chemogenomic view." Chemogenomics in Drug Discovery: A Medicinal Chemistry Perspective 22 (2006) ("Hendrix") at p. 247, Lines, T. C., and M. Ono. "FRS 1000, an extract of red onion peel, strongly inhibits phosphodiesterase 5A (PDE 5A)." Phytomedicine 13.4 (2006): 236-239 ("Lines") at p. 238, Murray, K. J., and P. J. England. "Inhibitors of cyclic nucleotide phosphodiesterases as therapeutic agents: Molecular and immunological approaches to the study of synaptic and axonal glycoproteins." Biochemical Society transactions 20.2 (1992): 460-464 ("Murray") at p. 460, Schudt, C., et al. (1996).

Claim No.	Claim Language	Description
		Phosphodiesterase Inhibitors, Academic Press at p. 41, and Thompson, W. Joseph. "Cyclic nucleotide phosphodiesterases: pharmacology, biochemistry and function." Pharmacology & therapeutics 51.1 (1991): 13-33 at p. 21.) Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.

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Claim No.	Claim Language	Description
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	

Exhibit A-10

"Antispasmodic effects of flavoxate, MFCA, and REC 15/2053 on smooth muscle of human prostate and urinary bladder"

("Caine")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Caine discloses a method of prophylaxis and treatment of benign prostatic hyperplasia. (*See, e.g.* p. 390, 393.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Caine teaches the use of Flavoxate compounds, potent PDE IV inhibitors, to relax prostatic tissues by inhibiting the action of intracellular PDE. Flavoxate compounds inhibit contractions and produce a relaxant effect on the smooth muscle of the human detrusor, prostatic adenoma, prostatic capsule, and bladder neck by direct action, believed to be via inhibition of the action of intracellular PDE. (*See, e.g.* pp. 392-393; Figure 5.) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of

[1] Caine, M., et al. "Antispasmodic effects of flavoxate, MFCA, and REC 15/2053 on smooth muscle of human prostate and urinary bladder." Urology 37.4 (1991): 390-394 ("Caine") was published on April 1, 1991.

Claim No.	Claim Language	Description
		PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-11

"A double-blind trial of an extract of the plant Serenoa repens in benign prostatic hyperplasia"

("Champault")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Champault discloses a method for prophylaxis or treatment of benign prostatic hyperplasia ("BPH"). (*See, e.g.*, p. 461-462.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Champault teaches the administration of an effective amount of the drug Permixon® (PA109), made from the hexane extract of *serenoa repens*, to treat BPH. (*See, e.g.* pp. 461-462, Table I.) *Serenoa repens* is a PDE V inhibitor. (*See, e.g.*, Yang, Surong, et al. "Saw Palmetto Extract Enhances Erectile Responses by Inhibition of Phosphodiesterase 5 Activity and Increase in Inducible Nitric Oxide Synthase Messenger Ribonucleic Acid Expression in Rat and Rabbit Corpus Cavernosum." Urology 81.6 (2013): 1380-e7.) **Table 1** Effect of treatment with PA109 on the objective and subjective signs of benign prostatic hyperplasia *Criteria* — n — *Before treatment* — *After treatment* — *% difference* — *Intragroup* P — *Intergroup* P Mean ± s.e. mean Nocturia (number of times): PA109 47, 3.12 ± 0.84, 1.69 ± 0.82, − 45.8, < 0.001; Placebo 41, 3.20 ± 0.77, 2.72 ± 0.89, − 15.0, < 0.001; < 0.001 Flow rate (ml/s): PA109 46, 5.35 ± 1.51, 8.05 ± 2.47, + 50.5, < 0.001; Placebo 39, 5.04 ± 1.64, 5.29 ± 2.10, + 5.0, NS; < 0.001 Post-micturition residue (ml): PA109 44, 94.7 ± 26.9, 55.1 ± 39.6, − 41.9, < 0.001; Placebo 34, 91.3 ± 45.2, 100.0 ± 60.9, + 9.3, NS; < 0.001 *Evaluations* — n — *Greatly improved* — *Improved* — *Unchanged or worsened* — χ^2 — P Dysuria: PA109 45, 16, 22, 7, 23.8, < 0.001; Placebo 44, 0, 22, 22 Patient self-rating: PA109 50, 11, 33, 6, 39.1, < 0.001; Placebo 44, 0, 30, 14 Physician's rating: PA109 50, 14, 31, 5, 53.4, < 0.001; Placebo 44, 0, 16, 28

[1] Champault, G., J. C. Patel, and A. M. Bonnard. "A double-blind trial of an extract of the plant Serenoa repens in benign prostatic hyperplasia." *British journal of clinical pharmacology* 18.3 (1984): 461-462. ("Champault") was published in September 1984.

Claim No.	Claim Language	Description
		Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Champault discloses the administration of Permixon® in combination with a pharmacologically acceptable excipient administered in a unit dose form of two tablets. (*See* p. 461.) Moreover, the use of the disclosed compound in combination

Claim No.	Claim Language	Description
		with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-12

"Characterization of a novel potent and specific inhibitor of type V phosphodiesterase"

("Coste")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Coste does not explicitly disclose the treatment of BPH. However, Coste teaches a method for increasing the intracellular concentration of cGMP for treatment of disorders that would benefit from the control of cGMP levels in smooth muscle cells. (*See, e.g.* pp. 1577; 1577-78 ("a powerful tool for enhancing cyclic nucleotide levels in cells;" 1583.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one,	Coste teaches the multiple mechanisms of action for increasing cGMP concentration in the cell to achieve smooth muscle relaxation in view of PDE activity. (*See, e.g.,* p. 1577.) Coste further teaches that most smooth muscle tissues can contain multiple isozymes of PDE, referencing tissue found in lungs, and vascular system. (*Id.*, p. 1583.) PDE V inhibitors include IBMX, Zaprinast and DMPPO. (*See, e.g.* pp. *passim*,1577-1583; Table 1.) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate,

[1] Coste, Hervé, and Pascal Grondin. "Characterization of a novel potent and specific inhibitor of type V phosphodiesterase." Biochemical pharmacology 50.10 (1995): 1577-1585. Received Feb. 28, 1995; accepted June 25, 1995. ("Coste") was published on November 9, 1995.

Claim No.	Claim Language	Description
	• 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-13

"Inhibitors of types I and V phosphodiesterase: Elevation of cGMP as a therapeutic strategy"

("Czarniecki")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Czarniecki discloses the prevention and treatment of various vascular smooth muscle disorders via the therapeutic manipulation of cGMP cell concentration levels. (*See, e.g.*, pp. 61, *passim.*)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one,	Czarniecki discloses the focus on PDE inhibition as a therapeutic target, including use of PDE V inhibitors such as Zaprinast, quinazolines, and other compounds for the treatment of cardiovascular diseases. (*See, e.g.*, p. 61; Table 1; pp. 65-69.) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time

[1]Czarniecki, Michael, Ho-Sam Ahn, and Edmund J. Sybertz. "Inhibitors of types I and V phosphodiesterase: Elevation of cGMP as a therapeutic strategy." *Annual reports in medicinal chemistry* 31 (1996): 61-70. ("Czarniecki") was published on October 14, 1996.

Claim No.	Claim Language	Description
	and pharmacologically compatible salts thereof.	of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-14

"Plant extracts in BPH"

("Di Silverio")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Di Silverio discloses a method for prophylaxis and treatment of benign prostatic hyperplasia. (*See, e.g.* pp.143, 147-149.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Di Silverio discloses a method of treatment wherein an effective amount of *Serenoa repens* is administered to a patient in need thereof. (*See, e.g.*, pp. 145, 147.) *Serenoa repens* has been demonstrated to inhibit PDE V. (*See, e.g.*, Yang, Surong, et al. "Saw Palmetto Extract Enhances Erectile Responses by Inhibition of Phosphodiesterase 5 Activity and Increase in Inducible Nitric Oxide Synthase Messenger Ribonucleic Acid Expression in Rat and Rabbit Corpus Cavernosum." Urology 81.6 (2013): 1380-e7.) Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including

[1] Di Silverio, F., et al. "Plant extracts in BPH." *Minerva urologica e nefrologica= The Italian journal of urology and nephrology* 45.4 (1993): 143-149. ("Di Silverio") was published in December 1993.

Claim No.	Claim Language	Description
		that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Di Silverio discloses the administration of *Serenoa repens* in combination with a pharmacologically acceptable excipient administered in a unit dose form. (*See* p. 145, 147.) Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-15

"N G-nitro-L-arginine inhibits non-adrenergic, non-cholinergic relaxation in rabbit urethral smooth muscle"

("Dokita")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Dokita reports that "[b]ladder emptying, micturition, is accompanied by an increase in intravesical pressure and concomitant decrease in outlet resistance." (p. 2429) Dokita teaches that "[t]he decrease in outlet resistance which accompanies micturition involves the inhibition of somatic neural efferents to the striated urethral sphincter, and the inhibition of alpha-adrenergically mediated smooth muscle sphincter tone. (p. 2429)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one,	Dokita discloses the use of a PDE V inhibitor. Dokita teaches the smooth muscle relaxation mechanism of bladder emptying, micturition, in the smooth muscle tissue of the urethra. (*See*, *e.g.*, p. 2429.) Dokita further teaches the increase in smooth muscle tissue relaxation using Zapranist (a cGMP inhibitor, i.e., a PDE V inhibitor) and methylene blue (and inhibitor of guanylate cyclase activity) along with electric field stimulation of urethra smooth muscle. (*See*, pp. 2431-2435.) The results demonstrate that the NANC-induced relaxation response in the urethra smooth muscle is related to NO biosynthesis and cGMP activity. Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed

[1] Dokita, Shinobu, et al. "N G-nitro-L-arginine inhibits non-adrenergic, non-cholinergic relaxation in rabbit urethral smooth muscle." Life sciences 48.25 (1991): 2429-2436. ("Dokita") was published in 1991.

Claim No.	Claim Language	Description
	• 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See*, *e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-16

"Alpha-1 receptor mediated smooth muscle regulation in benign prostatic hyperplasia"

("Drescher")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Drescher discloses a method for prophylaxis or treatment of benign prostatic hyperplasia ("BPH"). (*See, e.g.*, pp. 33, 34, and 38.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Drescher teaches that symptoms of BPH are partially caused by increased prostatic smooth muscle tone and that use of PDE inhibitors such as papaverine and theophylline (which are inhibitors of PDE V) increase smooth muscle relaxation in the prostate and should be investigated further for new therapeutic treatments of BPH and ED. (See pp. 33- 35, 36, Figure 4 and 38.) Drescher also discloses that the plant alkaloid ryanodine inhibits smooth muscle contractility as well as caffeine. (p. 37) Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the

[1] Drescher, P., et al. "Alpha-1 receptor mediated smooth muscle regulation in benign prostatic hyperplasia." Scan J. Urol Nephrol, Suppl.157 (1994). ("Drescher") was published in January 1994.

Claim No.	Claim Language	Description
		invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compounds in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-17

"Smooth muscle contractility in prostatic hyperplasia: role of cyclic adenosine monophosphate"

("Drescher 2")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Drescher 2 discloses methods for prophylaxis or treatment of BPH: "new therapeutic modalities focusing on relaxation of the prostatic smooth muscle may be beneficial" for the prevention and treatment of benign prostatic hyperplasia ("BPH"). (*See, e.g.*, p.76.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-	Drescher 2 teaches the use of theophylline and papaverine, both known to inhibit PDE V, to suppress smooth muscle contractions in the prostate. (*See, e.g.*, pp. 76, 77, 78 and 79) Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time

[1] Drescher, P., R. E. Eckert, and P. O. Madsen. "Smooth muscle contractility in prostatic hyperplasia: role of cyclic adenosine monophosphate." The Prostate 25.2 (1994): 76-80. ("Drescher 2") was published on August 08, 1994.

Claim No.	Claim Language	Description
	2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compounds in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-18

("Epimedium Herbs")
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Epimedium herbs (*e.g.*, Horny Goat Weed) have been used for centuries in a method for the prophylaxis and treatment of benign prostatic hyperplasia. (*See, e.g.*, Flaws, Bob, et al. "The treatment of modern Western medical diseases with Chinese medicine: a textbook & clinical manual." Blue Poppy Enterprises, Inc., 2001 ("Flaws") at pp. 91, 93, and 94.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	The method teaches the administration of an effective amount of epimedium herbs, which include as an active ingredient a PDE V inhibitor, to a person in need thereof. (*See, e.g.* the formulae taught in Flaws at pp. 91, 93, and 94; the administration of Horny Goat Weed (Epimedium Herbs) for more than 2000 years as taught in Kim, Sae Woong. "Phytotherapy: emerging therapeutic option in urologic disease." Translational Andrology and Urology 1.3 (2012): 181-191 ("Kim") at pp. 185-186; Kim also teaches that icariin, the active compound in epimedium herbs is a PDE V inhibitor (see Kim at pp. 185-186); this is also taught in Ma, Huiping, et al. "The genus Epimedium: an ethnopharmacological and phytochemical review." Journal of ethnopharmacology 134.3 (2011): 519-541 ("Ma") at p. 531 and *generally*, in Ning, Hongxiu, et al. "Effects of icariin on phosphodiesterase-5 activity in vitro and cyclic guanosine monophosphate level in cavernous smooth muscle cells." Urology 68.6 (2006): 1350-1354 ("Ning") at p. 1351 and *generally*, and in Xin, Z. C., et al. "Effects of icariin on cGMP-specific PDE5 and cAMP-specific PDE4 activities." Asian journal of andrology 5.1 (2003): 15-18 ("Xin"), *generally*. Horny Goat Weed (Epimedium Herbs) also contains quercetin, luteolin, naringenin, luteolin and kaempferol, which are also PDE

Claim No.	Claim Language	Description
		V inhibitors as shown in Ma at p. 531 and *generally*, Lines, T. C., and M. Ono. "FRS 1000, an extract of red onion peel, strongly inhibits phosphodiesterase 5A (PDE 5A)." Phytomedicine 13.4 (2006): 236-239 ("Lines") at pp. 236, 238, and *generally*, Ko, Wun-Chang, et al. "Inhibitory effects of flavonoids on phosphodiesterase isozymes from guinea pig and their structure–activity relationships." Biochemical pharmacology 68.10 (2004): 2087-2094 ("Ko") at pp. 2087, 2092 and *generally*, Orallo, Francisco, et al. "Implication of cyclic nucleotide phosphodiesterase inhibition in the vasorelaxant activity of the citrus-fruits flavonoid (+/-)-naringenin." Planta medica 71.2 (2005): 99-107 ("Orallo") at p. 99 and *generally*, and Yu, Ming-Chih, et al. "Luteolin, a non-selective competitive inhibitor of phosphodiesterases 1–5, displaced [3 H]-rolipram from high-affinity rolipram binding sites and reversed xylazine/ketamine-induced anesthesia." European journal of pharmacology 627.1 (2010): 269-275 ("Yu 3") at p. 269 and *generally*.) This treatment has been available and used for centuries to prevent and treat BPH. Due to translation issues, Defendants reserve the right to identify additional prior art references which show the extensive use of epimedium herbs which include a PDE V inhibitor and which anticipate and/or render obvious the claimed invention. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the

Claim No.	Claim Language	Description
		prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Epimedium herbs (*e.g.*, Horny Goat Weed) have been used for centuries in a method for the prophylaxis and treatment of benign prostatic hyperplasia in combination with a pharmacologically acceptable excipient that is administered in a unit dose form. (*See, e.g.* the formulae taught in Flaws at pp. 91, 93, and 94.) This treatment has been available and used for centuries to prevent and treat BPH. Due to translation issues, Defendants reserve the right to identify additional prior art references which show the extensive use of epimedium herbs which include a PDE V inhibitor and which anticipate and/or render obvious the claimed invention.

Exhibit A-19

United State Patent No. 5,721,238 ("Heiker '238")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Heiker '238 discloses a method for prophylaxis or treatment of "diseases of the urogenital system, such as, for example, prostate hypertrophy, impotence and incontinence." Col. 9:41-43.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Heiker '238 discloses various compounds that inhibit one or more of the cGMP-metabolizing phosphodiesterases (PDE I, PDE II and PDE V), including a "cGMP-specific PDE V", that are employed in medicaments to be administered to a person in need of treatment of urogenital diseases. Col. 9:19-43; col. 26:50-53, 62-65. One of ordinary skill in the art would know that PDE V inhibitors are cGMP-specific. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time

[1] U.S. Patent No. 5,721,238 ("Heiker '238") was filed on January 11, 1996, was issued on February 24, 1998, claims a priority date of January 19, 1995, and is titled "2,8-distributed quinazolinones"

Claim No.	Claim Language	Description
		of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Heiker '238 discloses compounds, including a cGMP-specific PDE V inhibitor, in combination with pharmacologically acceptable excipients administered in unit dose form. Col. 10:30-55. Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-20

"Clinical and retrospective evaluation of Eviprostat: a non-hormonal and non-neuropharmacological agent for benign prostatic hyperplasia"

("Ishigooka")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Ishigooka teaches a method for the prophylaxis and treatment of benign prostatic hyperplasia ("BPH"). (*See, e.g.*, Abstract; *see, also*, Tanaka, Tomoaki, et al. "Suppressive effects of Eviprostat, a phytotherapeutic agent, on lower urinary tract symptoms in prostate cancer patients treated with brachytherapy." LUTS: Lower Urinary Tract Symptoms 4.1 (2012): 25-28 ("Tanaka") at p. 25.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one,	Ishigooka teaches the administration to a person in need thereof of Eviprostat, an inhibitor of PDE V. Eviprostat has been successfully used as a non-hormonal and non-neuropharmacological treatment BPH in Japan. Clinically, Eviprostat subjectively relieved obstructive symptoms of BPH. Objective improvements were also demonstrated by ultrasonographic evaluation of prostatic volume and urinary flow rates. (*See* Ishigooka at pp. 61-62 and *generally*; Eviprostat contains equisetum arvense as shown in Tanaka at p. 25; equisetum arvense contains several components, including, quercetin, luteolin and kaempferol as shown in Veit, Markus, et al. "Interspecific and intraspecific variation of phenolics in the genus Equisetum subgenus Equisetum." Phytochemistry 38.4 (1995): 881-891 ("Veit") at p. 883 and *generally*; quercetin, luteolin and kaempferol are PDE V inhibitors as shown in Lines, T. C., and M. Ono. "FRS 1000, an extract of red onion peel,

[1] Ishigooka, M., et al. "Clinical and retrospective evaluation of Eviprostat: A non-hormonal and non-neuropharmacological agent for benign prostatic hyperplasia." International urology and nephrology 27.1 (1995): 61-66. ("Ishigooka") was published in 1995.

Claim No.	Claim Language	Description
	• 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	strongly inhibits phosphodiesterase 5A (PDE 5A)." Phytomedicine 13.4 (2006): 236-239 ("Lines") at pp. 236, 238, and *generally*, Ko, Wun-Chang, et al. "Inhibitory effects of flavonoids on phosphodiesterase isozymes from guinea pig and their structure–activity relationships." Biochemical pharmacology 68.10 (2004): 2087-2094 ("Ko") at pp. 2087, 2092 and *generally*, and Yu, Ming-Chih, et al. "Luteolin, a non-selective competitive inhibitor of phosphodiesterases 1–5, displaced [3 H]-rolipram from high-affinity rolipram binding sites and reversed xylazine/ketamine-induced anesthesia." European journal of pharmacology 627.1 (2010): 269-275 ("Yu 3") at p. 269 and *generally*.) Defendants reserve the right to amend this claim chart to include additional teachings from Ishigooka upon translation of the prior art reference. Defendants further reserve the right to identify additional prior art references which show the extensive use of Eviprostat in Asia, including Japan, which anticipate and/or render obvious the claimed invention. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time

Claim No.	Claim Language	Description
		of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Ishigooka discloses Eviprostat, a PDE V inhibitor, which can be administered with a pharmacologically acceptable excipient (which can include water) in unit dose form. Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. *See, e.g., The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995).*

Exhibit A-21

"Medical therapy for benign prostatic hyperplasia"

("Lepor 3")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Lepor 3 discloses medical therapies for the prophylaxis and treatment of benign prostatic hyperplasia. "Benign prostatic hyperplasia (BPH) describes a benign proliferative process of the stromal and epithelial elements of the prostate." (p. 483) "The clinical manifestations attributed to BPH include symptoms of prostatism, bladder dysfunction (deficient detrusor contractility/detrusor instability), urinary tract infection, urinary retention, renal insufficiency, and hematuria." (*Id.*). Lepor 3 notes that "[t]he goal of treatment for BPH is to relieve or reverse these clinical manifestations." (p. 484)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-	Lepor 3 discloses the use of pharmacological agents to treat BPH. Lepor 3 does not expressly disclose inhibitors of PDE V. Lepor 3 notes that "[p]harmacological agents designed to relax prostatic smooth muscle (alpha blockade) and reduce prostatic size (androgen suppression) have recently been reported to be a safe and effective treatment for BPH." (p. 485) Lepor 3 reviews the rationale for alpha blockade (relaxing the smooth muscle of prostate), androgen suppression and estrogen suppression for treatment of BPH. The compounds identified are all selective alpha blockers (terazosin) or antiandrogens (finasteride). (pp. 485-496) Lepor 3 also discloses the increasing role for medical therapy for BPH instead of surgical therapy (transurethral resection of the prostate, TURP). (p. 484) Lepor 3 teaches that future treatment of BPH may include "relaxation of

[1] Lepor, Herbert. "Medical therapy for benign prostatic hyperplasia." Urology 42/5 (1993): 483-501. ("Lepor 3") was published on January 12, 1995.

Claim No.	Claim Language	Description
	d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	smooth muscle in BPH may also be achieved by endothelin antagonists" and demonstrates motivation to look for and try various pharmacological agents to treat BPH ("The pharmaceutical industry is actively engaged in efforts to synthesize selective endothelin antagonists."). (p. 497) Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.

Lepor 3 vs. U.S. Patent No. 8,791,124

Claim No.	Claim Language	Description
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Lepor 3 discloses various pharmacologically acceptable ways to administer compounds to treat BPH in unit dose form. E.g., pp. 491, 494. Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-22

"Phytotherapy in treatment of benign prostatic hyperplasia: a critical review."

("Lowe 2")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Lowe 2 teaches a method for the prevention and treatment of benign prostatic hyperplasia ("BPH"). (*See, e.g.* pp. 12-18.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Lowe 2 teaches the administration to a person in need thereof of saw palmetto berry (*Serenoa repens*), which has been shown to inhibit PDE V. (*See,* Lowe 2 at p. 13 and *generally*; *see, also, e.g.*, Champault, G., J. C. Patel, and A. M. Bonnard. "A double-blind trial of an extract of the plant *Serenoa repens* in benign prostatic hyperplasia." British journal of clinical pharmacology 18.3 (1984): 461-462 ("Champault") *generally*, Di Silverio, F., et al. "Plant extracts in BPH." Minerva urologica e nefrologica= The Italian journal of urology and nephrology 45.4 (1993): 143-149 ("Di Silvero") at p. 143 and *generally*, Kim, Sae Woong. "Phytotherapy: emerging therapeutic option in urologic disease." Translational Andrology and Urology 1.3 (2012): 181-191 ("Kim") at p. 182-183, Narayan, Perinchery, and Ramaiah Indudhara. "Pharmacotherapy for benign prostatic hyperplasia." Western journal of medicine 161.5 (1994): 495 ("Narayan") at p. 498, Plosker, Greg L., and Rex N. Brogden. "Serenoa repens (Permixon®)." Drugs & aging 9.5 (1996): 379-395 ("Plosker") at p. 379 and *generally*, Rickards, D. and T. J. Christmas (1994). Benign prostatic hyperplasia: A Colour Guide, Graftham Press ("Rickards"), Roylance, P., B. Gibelin, and J. Espie. "Current treatment of BPH." Biomedicine & pharmacotherapy 49.7 (1995): 332-338 ("Roylance") at p. 334-335, and Yang, Surong, et al.

[1] Lowe, Franklin C., and James C. Ku. "Phytotherapy in treatment of benign prostatic hyperplasia: a critical review." Urology 48.1 (1996): 12-20. ("Lowe 2") was published in July 1996.

Claim No.	Claim Language	Description
		"Saw Palmetto Extract Enhances Erectile Responses by Inhibition of Phosphodiesterase 5 Activity and Increase in Inducible Nitric Oxide Synthase Messenger Ribonucleic Acid Expression in Rat and Rabbit Corpus Cavernosum." Urology 81.6 (2013): 1380-e7 ("Yang") at p. 1380(e7) and *generally*.) Defendants reserve the right to amend its disclosure to provide additional evidence of the PDE V capabilities of each of the identified compounds or compounds which fall within any genus identified in the prior art reference. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition

Claim No.	Claim Language	Description
		affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Lowe 2 discloses saw palmetto extract, *Serenoa repens*, which can be administered with a pharmacologically acceptable excipient (which can include water) in unit dose form. Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. *See, e.g., The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995).*

Exhibit A-23

United State Patent No. 5,171,217 ("March '217")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	March '217 discloses a method for prophylaxis or treatment of benign prostatic hypertrophy as well as clearing and restoring prostatic and other intrusions in the urethra. Col. 1:61-66; col. 2:30-41.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	March '217 discloses administering to a patient in need of treatment a drug "selected from a broad variety of drugs known to inhibit smooth muscle cell proliferation" including "phosphodiesterase inhibitors (e.g., isobutyl methylxanthine)." Col. 3:15-57. The disclosed PDE inhibitor, isobutyl methylxanthine (IBMX), inhibits PDE V. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time

[1] U.S. Patent No. 5,171,217 ("March '217") was filed on February 28, 1991, was issued on December 15, 1992, and is titled "Method for Delivery of Smooth Muscle Cell Inhibitors."

Claim No.	Claim Language	Description
		of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The compounds disclosed in March '217 may be used in combination with pharmacologically acceptable excipients administered in unit dose form. Col. 3:5-14; col. 4:9-63; col. 5:5-col. 6:8. The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-24

WO 94/12499 ("Matsuura '499")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Matsuura '499 discloses methods of treatment of various diseases, including renal failure (which is a symptom of BPH). (See, e.g., Lepor 3 at 483)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Matsuura '499 discloses administering to a patient in need of treatment 1,8-naphthyridin-2-one derivatives, which are disclosed to be effective as a therapeutic agent for various diseases by inhibiting PDE, including cGMP-specific PDE such as PDE V. (Specification, 2nd page) Matsuura '499 teaches that "[i]t has been known that PDE is widely distributed in tissues in living bodies and that PDE inhibitors inhibit PDE to increase cAMP and cGMP concentrations in cells, thereby providing various pharmacological actions. For example, a relaxing action on vascular smooth muscles and tracheal smooth muscles …." (*Id.*) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including

[1] WO 94/12499 ("Matsuura '499") was filed on December 1, 1992 and published on June 9, 1994.

Claim No.	Claim Language	Description
		that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-25

"Medical Treatment of Benign Prostatic Hyperplasa: 5α-Reductase Inhibitors and α-Adrenergic Antagonists"

("Monda")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Monda discloses methods for prophylaxis or treatment of BPH. Monda reports on the use of two medical treatments for BPH in lieu of surgical intervention: 5α-reductase inhibitors and α-adrenergic antagonists.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one,	Monda discloses that α-adrenergic antagonists inhibit the adrenergic receptors located in the prostatic adenoma, prostatic capsule, and bladder neck and decrease the smooth muscle tone of these structures. By decreasing the resistance to urine flow through the bladder neck and prostatic urethra, the patient's ability to urinate can improve. (p. 674) Monda also teaches that the human BPH tissue consists primarily of stroma rich in smooth muscle, medical treatments such as α-adrenergic antagonists should be able to decrease bladder outflow resistance and thereby be effective in the treatment of BPH. (p. 675) Monda thus provides motivation to persons skilled in the art to apply other medical treatments known to relax smooth muscle (such as PDE V inhibitors) to treat BPH. Monda emphasizes the importance of medical treatments in lieu of the surgical option (transurethral resection of the prostate, or TURP) for several reasons, including the expense, the associated morbidity, and reduced life expectancy. Because of these concerns [with transurethral

[1] Jeffrey M. Monda and Joseph E. Oesterling, Medical Treatment of Benign Prostatic Hyperplasia: 5α-Reductase Inhibitors and α-Adrenergic Antagonists, Mayo Clin Proc 1993; 68:670-679.

Claim No.	Claim Language	Description
	and pharmacologically compatible salts thereof.	resection of the prostate], interest in the development of medical therapies for the management of symptomatic BPH has flourished in recent years. This activity has been fueled by (1) the medical community's quest to develop an alternative treatment for such a common condition, (2) the inordinate cost associated with the current surgical approach, (3) the federal government's attempt to control health-care costs, and (4) the patient's desire to avoid surgical treatment and its associated risks. Because of the high prevalence of BPH in our aging population, feasible, low-risk, effective and cost-efficient options are necessary. Clearly, the 1990s represents a transition period during which the management of symptomatic BPH is more more medical and less surgical. (p. 671) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of

Claim No.	Claim Language	Description
		PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Monda discloses clinical studies using finasteride in combination with pharmacologically acceptable excipients administered in unit dose form (pp. 672-73) as well as α-adrenergic antagonists (pp. 675-77) Moreover, the use of PDE V inhibitor compounds in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. *See, e.g., The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995).*

Exhibit A-26

CA 2,084,962 ("Morioka '962")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Morioka '962 discloses a method for prophylaxis or treatment of dysuria, including incontinence of urine, such as by prolonging urination intervals and increasing urination threshold pressure. Abstract, ll. 19-24. "This invention relates to novel pharmaceutical compositions for the improvement of dysuria such as pollakiuia or incontinence of urine. Dysuria is often caused by adult diseases such as cerebrovascular disorders and prostatic diseases…." (Field of Invention, ll. 5-9)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one,	Morioka '962 discloses administering to a patient in need of treatment novel xanthine derivatives to directly relax cystic smooth muscles due to inhibitory actions of adenosine uptake as as well as of cAMP and cGMP phosphodiesterase activities. (p. 5, ll. 19-30) The disclosed compound propentofylline is known to inhibit PDE V. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention.

[1] Canadian patent application CA 2,084,962 ("Morioka '962") was filed on December 9, 1992, published on June 11, 1993, and is titled "Pharmaceutical Composition for the Improvement of Dysuria."

Claim No.	Claim Language	Description
	• 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The compounds disclosed in Morioka '962 may be used in combination with pharmacologically acceptable excipients administered in unit dose form. The reference teaches methods of administration can be oral, intravenous, subcutaneous, intramuscular and rectal and the drug can be administered in various formulations at disclosed dosages. (p. 6, ll. 1-14; p. 7, ll. 12-14)

Exhibit A-27

"Phosphodiesterase VA Inhibitors"

("Murray 2").[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Murray 2 teaches the use of inhibitors of PDE V for the prophylaxis or treatment of various diseases based upon the known mechanism of action of smooth muscle relaxation. (pp. 152-53) Murray does not expressly disclose the treatment of BPH; however, one of ordinary skill in the art would be motivated to use, and would find it obvious to use, known inhibitors of PDE V for relaxation of smooth muscle to induce relaxation of smooth muscle in the prostrate known to prevent or treat BPH.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-	Murray 2 teaches that "Cyclic nucleotide phosphodiesterases (PDEs) have long been regarded as potential targets for therapeutic agents. More recently, interest in this area has been renewed by the recognition that there are five distinct PDE isoenzyme families, and that tissues have different complements of these isoenzymes. There is, therefore, a logical foundation for selective PDE inhibitors to be used to increase cyclic nucleotide levels in specific target tissues or organs. Indeed, selective PDE III inhibitors…are currently used clinically for the treatment of congestive heart failure and as antithrombotic agents, and this success has given hope that inhibitors of PDE isoenzymes will also be useful drugs." (p. 150) Murray 2 further teaches that PDE V is a cGMP-specific PDE isoenzyme, that its function is very similar in all of the tissues in which it has been found, and that PDE V is specific for cGMP as a substrate, *i.e.* it will not affect cAMP levels. (pp. 150-151)

[1] Murray, Kenneth J. "Phosphodiesterase VA Inhibitors." *Drug News and Perspectives* 6 (1993): 150-156 ("Murray 2") was published in April 1993.

Claim No.	Claim Language	Description
	propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Murray 2 discloses that PDE V inhibitors (e.g., Zaprinast) have been shown to relax a variety of vascular smooth muscles. This effect has also been shown in trachea and airway smooth muscle, lower esophageal sphincter muscle; colon muscle, gastric fundus and the corpus cavernosum. There, Zaprinast enhanced relaxation caused by nitric oxide or electrical stimulation. (pp. 151-153) Murray 2 discloses other known PDE Va inhibitors, including MY-5445; dipyridamole; papaverine and certain methylxanthines, including IBMX and 8-MeO-IBMX; theophylline and disodium cromoglycate. **TABLE IV: PDE V_A INHIBITORS[a]** TISSUE: LUNG (BOV, BOV, PIG, HUM); PLATELET (HUM, BOV, MON); AORTA (RAB, RAT); TRACHEA (DOG) SPECIES[b]: BOV, BOV, PIG, HUM, HUM, BOV, MON, RAB, RAT, DOG REFERENCE: 13, 53, 18, 55, 42, 54, 17, 13, 19, 16 IC_{50} (mcM) Zaprinast: 0.5, 0.3, 0.9, 1.1, 0.1, 0.3, 0.5, 0.2, 0.1 MY-5445: 0.6, 1.3 SK&F-96231: 1.0 Dipyridamole: 3, 0.8, 1.0, 0.4, 7, 2.5 Papaverine: 9, 9 IBMX: 8, 3.4, 2.2, 6, 0.8 8-MeO-IBMX: 2.5, 6, 10, 10, 7.5 MIMAX: 0.4 Theophylline: 250, >100, 160, 280, 200, 42 DSCG: >100, 250 Cicletanine: 375 [a]PDE V_A was purified or partially purified from the tissues or cells shown. As different conditions were used to determine the IC_{50} values, the results for a particular inhibitor are not comparable for the different tissues. The table shows the relative potencies of PDE V_A inhibitors as determined by each group. [b]BOV, bovine; HUM, human; MON, monkey; RAB, rabbit. (p. 154) Murray 2 reference teaches that "[s]mooth muscle relaxation appears to be the most promising of the potential uses of PDE Va inhibitors, and possible therapeutic utilities could include vasodilation, bronchodilation, modulation of gastrointestinal motility and treatment of impotence." (pp. 154-155)

Claim No.	Claim Language	Description
		Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The

Claim No.	Claim Language	Description
		Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-28

"Pharmacotherapy for benign prostatic hyperplasia"

("Narayan")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Narayan discloses methods for the prophylaxis or treatment of benign prostatic hyperplasia. Narayan discusses the pathophysiology of BPH symptoms noting that BPH develops in the transition zone, which is adjacent to the urethra. (See also: Figure 1) The reference notes, "The benign enlargement of the transition zone is called prostatic adenoma. Enlargement of the prostate may compress the urethra and block the free egress of urine during micturition…..The symptom complex associated with BPH is called prostatism." (pp. 496-97) Narayan teaches that stromal tissue is an important component of BPH; such tissue may be composed of varying amounts of smooth muscle and fibrous connections. "In addition, the prostatic urethra and bladder neck have a substantial amount of smooth muscle that comes into play in causing symptoms of BPH." (p. 500) Narayan also describes many symptoms of BPH and teaches that the current pharmacotherapy for BPH is based on agents that relax the smooth muscles of prostatic urethra and stroma and those that deprive acinar cells of androgen. Narayan reviews alpha blocker therapy and androgen suppression therapy, including the combination of the two. (pp. 496-504)
1. (b)	administering to a person in need thereof an effective amount of	Narayan teaches that the current pharmacotherapy for BPH is

[1] Narayan, Perinchery, and Ramaiah Indudhara. "Pharmacotherapy for benign prostatic hyperplasia." Western journal of medicine 161.5 (1994): 495-506. ("Narayan") was published in November 1994.

Claim No.	Claim Language	Description
	an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	based on agents that relax the smooth muscles of prostatic urethra and stroma and those that deprive acinar cells of androgen. Narayan reviews alpha blocker therapy and androgen suppression therapy, including the combination of the two. (pp. 496-504) Narayan does not expressly disclose inhibitors of PDE V; however, a person of skill in the art would be motivated and find it obvious to substitute known inhibitors of PDE V for the relaxation of smooth muscle for known pharmacological treatments for BPH based upon relaxation of smooth muscle (e.g., alpha blockers). Indeed, Narayan emphasizes the "intensive search for alternative therapies [to surgical therapy] for prostatic hyperplasia." p. 495 (abstract). "There has recently been an explosion of interest in the medical management of BPH." (p. 505) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or

Claim No.	Claim Language	Description
		treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-29

United States Patent No. 5,861,396

("Niewohner '396")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Niewohner '396 discloses methods for prophylaxis or treatment of cardiovascular disorders, disorders of the vascular system and of the urogenital system. Abstract; col. 1:3-7. "An increase in the cGMP level can lead to antithrombotic, vasodilatory, antiarrhythmic and/or anti-inflammatory action …. In addition, compounds of the invention enhance the effect of substances such as EDRF (endothelium-derived relaxing factor)….which increases the cGMP level. As a result, the compounds' "relaxing action on the smooth musculature makes them suitable for the treatment of disorders of the urogenital system such as prostate hypertrophy, impotence and incontinence." Col. 12:8-12.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-	Niewohner '396 discloses administration of 9-substituted 2-(2-n-alkoxyphenyl)-purin-6 ones and their use as medicaments for the treatment of inflammations, thromboembolic and cardiovascular diseases and diseases of the "urogenital system." The reference notes that purinone and quinazolones are known as selective cGMP PDE inhibitors and that PDEs "play an essential role in the regulation of the intracellular cGMP and cAMP levels" with PDE I, II and V "essentially responsible for the metabolism of cGMP." "Due to the distribution of these cGMP metabolizing PDEs in tissue, selective inhibitors should, depending on the tissue distribution of the corresponding isoenzyme raise cGMP levels in the corresponding tissue. This can lead to specific, antiaggregatory, antispastic, vasodilating, antiarrhythmic and/or

[1] United States Patent No. 5,861,396 ("Niewohner '396") was filed on October 30, 1996, with a priority date of November 6, 1995, issued on January 19, 1999, and is titled "Purin-6-one derivatives."

<table>
<tr><th>Claim No.</th><th>Claim Language</th><th>Description</th></tr>
<tr><td></td><td>imidazole,
• 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one,
• 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one,
• 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one,
and pharmacologically compatible salts thereof.</td><td>anti-inflammatory action." Col. 1:6-21. Niewohner '396 specifically discloses a PDE V inhibitor. Col. 12:14-55.

<table>
<tr><th>Ex. No.</th><th>PDE I IC_{50} [nM]</th><th>PDE II IC_{50} [nM]</th><th>PDE V IC_{50} [nM]</th></tr>
<tr><td>1</td><td>500</td><td>200</td><td>300</td></tr>
<tr><td>33</td><td>3000</td><td>100</td><td>800</td></tr>
<tr><td>34</td><td>~500</td><td>20</td><td>500</td></tr>
<tr><td>69</td><td>3000</td><td>60</td><td>500</td></tr>
<tr><td>80</td><td>100</td><td>80</td><td>1000</td></tr>
<tr><td>82</td><td>100</td><td>20</td><td>500</td></tr>
<tr><td>83</td><td>300</td><td>20</td><td>500</td></tr>
<tr><td>84</td><td>100</td><td>20</td><td>1000</td></tr>
</table>
-continued
<table>
<tr><th>Ex. No.</th><th>PDE I IC_{50} [nM]</th><th>PDE II IC_{50} [nM]</th><th>PDE V IC_{50} [nM]</th></tr>
<tr><td>100</td><td>1000</td><td>4</td><td>1000</td></tr>
<tr><td>121</td><td>500</td><td>3</td><td>1000</td></tr>
<tr><td>122</td><td>500</td><td>4</td><td>1000</td></tr>
<tr><td>138</td><td>500</td><td>1</td><td>500</td></tr>
</table>

Claim 4 expressly recites a "method for treating hypertrophy in a patient in need thereof which comprises administering to said patient an effective amount" of a compound as disclosed therein, including a PDE V inhibitor.

Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention.</td></tr>
</table>

Claim No.	Claim Language	Description
		There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Niewohner '396 discloses the dosages used and various methods of administration of the dosage, with a preferred administration and dosage level. Col. 13:15-51.

Exhibit A-30

United States Patent No. 5,861,404

("Niewohner '404")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Niewohner '404 discloses methods for prophylaxis or treatment of cardiovascular disorders, disorders of the vascular system and of the urogenital system. Abstract; col. 1:3-7. "An increase in the cGMP level can lead to antithrombotic, vasodilatory, antiarrhythmic and/or anti-inflammatory action …. In addition, compounds of the invention enhance the effect of substances such as EDRF (endothelium-derived relaxing factor)….which increases the cGMP level." Col. 6:50-60. As a result, the compounds are disclosed for the treatment of "diseases of the urogenital system such as prostate hypertrophy, impotence and incontinence." Col. 7:5-7.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole,	Niewohner '404 discloses administration of 9-substituted 2-(2-n-alkoxyphenyl)-purin-6 ones and their use as medicaments for the treatment of inflammations, thromboembolic and cardiovascular diseases and diseases of the "urogenital system." The reference notes that purinone and quinazolones are known as selective cGMP PDE inhibitors and that PDEs "play an essential role in the regulation of the intracellular cGMP and cAMP levels" with PDE I, II and V "essentially responsible for the metabolism of cGMP." "Due to the distribution of these cGMP metabolizing PDEs in tissue, selective inhibitors should, depending on the tissue distribution of the corresponding isoenzyme raise cGMP levels in the corresponding tissue. This can lead to specific, antiaggregatory, antispastic, vasodilating, antiarrhythmic and/or anti-inflammatory action." Col. 1:22-36. Niewohner '404

[1] United States Patent No. 5,861,404 ("Niewohner '404") was filed on January 12, 1996, issued on January 19, 1999, and is titled "2,9-distributed purin-6-ones."

Claim No.	Claim Language	Description
	• 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	specifically discloses a PDE V inhibitor. Col. 7:13-48. Inhibition of the phosphodiesterases in vitro Example No. / PDE I IC_{50} [μM] / PDE II IC_{50} [μM] / PDE V IC_{50} [μM] 5 / 10 / 3 / 50 8 / 40 / 2 / 14 / 4 / 0.6 / 0.3 20 / 1 / 0.4 / 1 25 / 3 / 0.1 / 10 Claim 4 expressly recites a "method for treating hypertrophy in a patient in need thereof which comprises administering to said patient an effective amount" of a compound as disclosed therein, including a PDE V inhibitor. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate,

Claim No.	Claim Language	Description
		with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person’s own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the ‘124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Niewohner ‘404 discloses the dosages used and various methods of administration of the dosage, with a preferred administration and dosage level. Col. 8:2-30.

Exhibit A-31

WO 96/32379

("Oku '379")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Oku '379 discloses a method for prophylaxis or treatment of diseases of the genitourinary system, including renal failure, glomerular diseases, and renal turbo-interstitial diseases. (pp. 35-38) One or skill in the art would know that the diseases of the genitourinary system, including renal failure and glomerular diseases, encompass prostatic diseases such as benign prostatic hyperplasia.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-	Oku '379 discloses administering to a patient in need of treatment cyclic nucleotide-PDE inhibitors, (*see* pp. 38-39), including "cGMP-specific family, selectively inhibited by Zaprinast (Type V)." Page 39, ll. 25-26. Oku '379 also discloses other inhibitors of PDE V, including papaverine and dipyridamole. (p. 37) Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention.

[1] WO 96/32379 ("Oku '379") was filed on April 2, 1996, with a priority date of April 10, 1995, published on October 17, 1996, and is titled "Indole Derivatives as cGMP-PDE Inhibitors."

Claim No.	Claim Language	Description
	propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The cyclic nucleotide-PDE inhibitors of Oku '379 can be administered in combination with pharmacologically acceptable excipients in unit dose form. Pages 40-42.

Exhibit A-32

("Onion")
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Onion has been eaten for centuries. Since at least 1991, eating onion has been believed to be a method for the prophylaxis and treatment of benign prostatic hyperplasia. (*See*, *e.g.*, Galeone, Carlotta, et al. "Onion and garlic intake and the odds of benign prostatic hyperplasia." Urology 70.4 (2007): 672-676. ("Galeone") at p. 672 and *generally*; *see*, *also*, Denis, L., M. S. Morton, and K. Griffiths. "Diet and its preventive role in prostatic disease." European urology 35.5-6 (1999): 377-387 ("Denis") at p. 377.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one,	The method teaches the administration of an effective amount of onions, which include as an active ingredient a PDE V inhibitor, to a person in need thereof. (*See*, *e.g.* Galeone at p. 672 and *generally* and Denis at p. 377; onion contains flavonoids and luteolin which are PDE V inhibitors (*see* Lines, T. C., and M. Ono. "FRS 1000, an extract of red onion peel, strongly inhibits phosphodiesterase 5A (PDE 5A)." Phytomedicine 13.4 (2006): 236-239 ("Lines") at p. 236 and *generally*, Denis at p. 377 and Formica, J. V., and W. Regelson. "Review of the biology of quercetin and related bioflavonoids." Food and chemical toxicology 33.12 (1995): 1061-1080 ("Formica") at pp. 1062 and 1071, Ko, Wun-Chang, et al. "Inhibitory effects of flavonoids on phosphodiesterase isozymes from guinea pig and their structure–activity relationships." Biochemical pharmacology 68.10 (2004): 2087-2094 ("Ko") at pp. 2087, 2092 and *generally*, and Yu, Ming-Chih, et al. "Luteolin, a non-selective competitive inhibitor of phosphodiesterases 1–5, displaced [3 H]-rolipram from high-affinity rolipram binding sites and reversed xylazine/ketamine-induced anesthesia." European journal of pharmacology 627.1 (2010): 269-275 ("Yu 3") at p. 269 and *generally*.)

Claim No.	Claim Language	Description
	and pharmacologically compatible salts thereof.	Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Onion has been eaten for centuries. Since at least 1991, eating onion has been believed to be a method for the prophylaxis and treatment of benign prostatic hyperplasia in combination with a pharmacologically acceptable excipient that is administered in a

Claim No.	Claim Language	Description
		unit dose form. (*See, e.g.* Galeone at p. 675.)

Exhibit A-33

WO/1995/018097

("Ozaki '097")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Ozaki '097 discloses a method for prophylaxis or treatment of diseases against which cGMP-PDE inhibitory action is effective. Ozaki '097 does not specifically disclose the treatment of benign prostatic hyperplasia, but one or skill in the art that the known effect of cGMP-PDE inhibitor action relaxes smooth muscle cells and that a known treatment of BPH was based on the relaxation of smooth muscle cells in the genitourinary system, including, for example, the prostate.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one,	The reference teaches an anthranilic acid derivative having a cGMP-PDE inhibitory activity. The reference discloses that it is well known that cGMP has a relaxant activity on vascular and bronchial smooth muscles. With that knowledge the inventors "directed their attention to an inhibitor activity against cGMP phosphodiesterase… and have studied on compounds having such an activity for many years." (The reference states that the anthranilic acid compound has inhibitory activity against PDE, "particularly cGMP-PDE. Accordingly, the anthranilic acid derivative of the present invention is effective in the prevention and treatment of diseases wherein a cGMP-PDE inhibitory action is efficacious." E.g., Claim 4 (claims use of compound for treating and preventing any disease wherein a cyclic GMP phosphodiesterase inhibitor action is efficacious."). The reference reiterates that any disease wherein cGMP-PDE inhibitory action is efficacious and lists certain diseases for which the disclosed

[1] WO/1995/018097 ("Ozaki '097") was filed on December 27 1994, with a priority date of December 27, 1993, published on July 6, 1995, and is titled "Anthranilic Acid Derivative."

Claim No.	Claim Language	Description
	• 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	compounds are particularly efficacious. Finally, the reference teaches various methods of administration and preferred and suggested dosages depending on the method of administration. Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1
3. (b)	wherein the compound in combination with a pharmacologically	The use of the disclosed compound in combination with a

Claim No.	Claim Language	Description
	acceptable excipient is administered in a unit dose form.	pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-34

"Non-adrenergic, non-cholinergic relaxation and levels of cyclic nucleotides in rabbit lower urinary tract"

("Persson")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Persson discloses the underlying mechanism of action for the prophylaxis or treatment of benign prostatic hyperplasia, namely that of the relaxation of the lower urinary tract smooth muscle. Persson discloses that nitric oxide (NO) has been proposed to produce relaxation of the smooth muscle of the bladder neck/trigone and urethra. (159) NO also appears to have a role as a messenger molecule in this region. NO activates cytosolic guanylate cyclase by heme-dependent mechanisms, resulting in cyclic GMP formulation. If NO, or a NO-related substance, is released from NANC nerves and reaches the muscle cells of the bladder outlet, an increase in cyclic GMP accumulation should be expected following NANC nerve stimulation as well as in response to administration of exogenous NO. Such an increase in cyclic GMP accumulation in response to NANC nerve stimulation has been demonstrated in various other tissues include penis muscle, lower oesophageal sphincter, anococcygeus muscle and proximal colon and corpus cavernosum. (159-60, 164) The study of Persson thus determines that "NO and NO-related drugs have relaxant effect on lower urinary tract smooth muscle, indirectly suggesting that the functional second messenger for NO, cyclic GMP, is present in lower urinary tract tissue." (164) "Nerve mediated urethral relaxation was found to increase the

[1] Persson, Katarina, and Karl-Erik Andersson. "Non-adrenergic, non-cholinergic relaxation and levels of cyclic nucleotides in rabbit lower urinary tract." European Journal of Pharmacology: Molecular Pharmacology 268.2 (1994): 159-167. ("Persson") was published in July 1994.

Claim No.	Claim Language	Description
		smooth muscle content of cyclic GMP by approximately 100%." *Id.*
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Persson discloses Zaprinast, an inhibitor of PDE V, and notes that it has been reported that Zaprinast potentiates the amplitude of relaxation in the urethra of a rabbit. (160) Persson evaluates the effect of Zaprinast in the detrusor and urethral tissue of rabbits, concluding the cGMP effect and relaxation of smooth muscle was effective in the urethra. Persson does not expressly disclose the administering of an inhibitor of PDE V to a person in need of treatment for BPH; however, a person of skill in the art would conclude from the teachings of Persson that an inhibitor of PDE V, given its effect on cGMP and relaxation of the lower urinary tract smooth muscle, would be obvious to use in a person to potentiate the lower urinary tract smooth muscle relaxation in order to treat BPH. Thus, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of

Claim No.	Claim Language	Description
		lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Persson discloses that the PDE V compound in combination with a pharmacologically acceptable excipient and administered in unit dose form. (p. 161, "2.5 Drugs and Solutions") Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-35

United States Patent No. 6,207,666 ("Piazza '666")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Piazza '666 discloses a method of treating a patient having a disease which would benefit from regulation of apoptosis by treating the patient with an effective amount" of one formulation. "The regulation of apoptosis is believed to play an important role in diseases associated with abnormalities of cellular growth patterns such as benign prostatic hyperplasia …." (Col. 5:40-43)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one,	Piazza '666 discloses treating a patient having a disease which would benefit from regulation of apoptosis by administering to the patient an effective amount of the compound of "formula [I]" disclosed therein. (Col. 5:37-40) The compound of formula [I] includes an inhibitor of PDE IV. It would have been obvious to a person of skill in the art to substitute an inhibitor of PDE V for the regulation of apoptosis to inhibit abnormalities of cellular grown such as benign prostatic hyperplasia. Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention.

[1] United States Patent No. 6,207,666 ("Piazza '666") was filed on April 23, 1998, as a continuation of application No. 08/473,094 filed on June 7, 1995, issued March 27, 2001 and is titled "Method for treating a patient having precancerous lesion with 4-phenylphthalazine derivatives."

Claim No.	Claim Language	Description
	and pharmacologically compatible salts thereof.	There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Piazza '666 discloses the dosages used and various methods of administration of the dosage, with a preferred administration and dosage level. Col. 5:54-6:28. Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-36

United States Patent No. 5,858,694 ("Piazza '694")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Piazza '694 discloses a method of treating a patient having a disease which would benefit from regulation of apoptosis by treating the patient with an effective amount" of one formulation. "The regulation of apoptosis is believed to play an important role in diseases associated with abnormalities of cellular growth patterns such as benign prostatic hyperplasia …." Col. 5:40-43.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one,	Piazza '694 discloses treating a patient having a disease which would benefit from regulation of apoptosis by administering to the patient an effective amount of the compound of "formula [I]" disclosed therein. Col. 5:37-40. The compound of formula [I] includes an inhibitor of PDE IV. It would have been obvious to a person of skill in the art to substitute an inhibitor of PDE V for the regulation of apoptosis to inhibit abnormalities of cellular grown such as benign prostatic hyperplasia. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention.

[1] United States Patent No. 5,858,694 ("Piazza '694") was filed on May 30, 1997, issued on January 12, 1999, and is titled "Method for Identifying Compounds for Inhibition of Cancerous Lesions."

Claim No.	Claim Language	Description
	and pharmacologically compatible salts thereof.	There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Piazza '694 discloses the dosages used and various methods of administration of the dosage, with a preferred administration and dosage level. Col. 5:54-6:28. Moreover, The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-37

United State Patent No. 6,200,980 ("Piazza '980")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Piazza '980, at column 5, line 63 through column 6, line 3 discloses a method for prophylaxis or treatment of benign prostatic hyperplasia. "[The] invention is a method of treating a patient having a disease which would benefit from regulation of apoptosis by treating the patient with an effective amount of the compound of Formula [I] above. The regulation of apoptosis is believed to play an important role in diseases associated with abnormalities of cellular growth patterns such as benign prostatic hyperplasia,…" Formula [I] is a phenylcycloaminopyrazolopyrimidinone.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one,	Piazza '980 discloses phenylcycloaminopyrazolopyrimidinones. (See Formula I, Examples 13 through 28, 51, 59, 64 through 103, 110, 111 and 113 through 152 Pyrazolopyrimidiones, such as sildenafil, are inhibitors of phosphodiesterase (PDE) V. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention.

[1] U.S. Patent No. 6,200,980 ("Piazza '980") was filed on April 17, 1997, was issued on March 13, 2001, claims a priority date of June 7, 1995, and is titled "Method of treating a patient having precancerous lesions with phenyl purinone derivatives."

Claim No.	Claim Language	Description
	• 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The pharmaceutically acceptable carrier and compounds of Formula I are formulated into unit dosage forms for administration to a patient. See, for example, column 5, lines 42 through 44.

Exhibit A-38

"Serenoa repens (Permixon®)"

("Plosker")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Plosker discloses a method for the prophylaxis or treatment of benign prostatic hyperplasia using saw palmetto extract, also known as Serenoa repens.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Plosker reports that Serenoa repens (Permixon®) has been available for several years for the treatment of men with benign prostatic hyperplasia (BPH). (379) The drug is the n-hexane lipidosterolic extract of the dwarf American palm (also known as Serenoa repens) and is a complex mixture of various compounds. *Id.* Serenoa repens (saw palmetto extract) is reported to inhibit PDE V. *See* Yang, Surong, et al. "Saw Palmetto Extract Enhances Erectile Responses by Inhibition of Phosphodiesterase 5 Activity and Increase in Inducible Nitric Oxide Synthase Messenger Ribonucleic Acid Expression in Rat and Rabbit Corpus Cavernosum." *Urology* 81.6 (2013): 1380-e7. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the

[1] Plosker, Greg L., and Rex N. Brogden. "Serenoa repens (Permixon®)." *Drugs & aging* 9.5 (1996): 379-395 ("Plosker") was published November 1, 1996.

Claim No.	Claim Language	Description
		prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Plosker reports on controlled clinical trials in men with BPH in which oral administration of Serenoa repens 160 mg twice daily for 1 to 3 months was generally superior to placebo in improving subjective symptoms, such as dysuria, as well as objective parameters. The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-39

("Pomegranate Juice")
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Pomegranate juice is used in a method for the prophylaxis and treatment of benign prostatic hyperplasia. (*See, e.g.*, Rajfer, Jacob. "Pomegranate juice: is it the new, all-natural phosphodiesterase type 5 inhibitor?" Reviews in urology 10.2 (2008): 168. ("Rajfer 2") at p. 169 and *generally*.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	The method teaches the administration of an effective amount of Pomegranate Juice, which contains a PDE V inhibitor, to a person in need thereof. (*See, e.g.* Rajfer 2 at pp. 168-169 and *generally*.) Defendants reserve the right to identify additional prior art references which show the extensive use of Pomegranate Juice which is a PDE V inhibitor and which anticipates and/or renders obvious the claimed invention. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE

Claim No.	Claim Language	Description
		V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Pomegranate juice contains a PDE V inhibitor, which can be administered with a pharmacologically acceptable excipient (which can include water) in unit dose form. Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. *See, e.g., The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995).*

Exhibit A-40

"Nitric oxide as a mediator of relaxation of the corpus cavernosum in response to nonadrenergic, noncholinergic neurotransmission"

("Rajfer")
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Rajfer teaches a method for the prophylaxis and treatment of erectile dysfunction ("ED"). (*See, e.g.* p. 94) A person of skill in the art would know that ED is a genitourinary disease, as is BPH.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Rajfer teaches the administration of a PDE V inhibitor, methylene blue or M& B 22,948, to relax the smooth muscle tissue of the corpus cavernosum by increasing intracellular concentration of cGMP. Further, Rajfer teaches that nitric oxide ("NO") also leads to smooth muscle relaxation in the corpus cavernosum by increasing the concentration of cGMP, that permits penile erection. (*See, e.g.*, 90, 94) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of

Claim No.	Claim Language	Description
		PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-41

("Red Wine")
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Red wine has been used for centuries for its health giving attributes. (*See, e.g.*, Finkel, H. E. (1995). "Book Review." New England Journal of Medicine 332(5): 340-340. ("Finkel") at p. 339.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Red wine includes as an active ingredient a PDE V inhibitor. (*See, e.g.* Dell'Agli, Mario, et al. "In vitro inhibition of human cGMP-specific phosphodiesterase-5 by polyphenols from red grapes." Journal of agricultural and food chemistry 53.6 (2005): 1960-1965 ("Dell'Agli") at p. 1960 and *generally*.) Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or

Claim No.	Claim Language	Description
		treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	

Exhibit A-42

"Benign prostatic hyperplasia: A Colour Guide"

("Rickards")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Rickards teaches a method for the prophylaxis and treatment of benign prostatic hyperplasia ("BPH".) Rickards provides an entire chapter on medical treatment for BPH. (pp. 65-73.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Rickards teaches the administration of an effective amount of saw palmetto extract, *Serenoa repens*, which has been demonstrated to inhibit PDE V. (*See, e.g.* p. 69.) (*See, e.g.*, Yang, Surong, et al. "Saw Palmetto Extract Enhances Erectile Responses by Inhibition of Phosphodiesterase 5 Activity and Increase in Inducible Nitric Oxide Synthase Messenger Ribonucleic Acid Expression in Rat and Rabbit Corpus Cavernosum." Urology 81.6 (2013): 1380-e7.) Rickards also teaches the administration of other medical agents for the treatment of BPH, including endocrine therapy (pp. 65-68) and alpha-adrenoceptor blockers (pp. 69-73). Rickards notes that at least 50% of the prostate stroma is smooth muscle, and teaches that alpha blockers mediate contraction of that smooth muscle with therapeutic effect on BPH. Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods

[1] D. Rickards, T.J. Christmas, "Benign Prostatic Hyperplasia: A Colour Guide", 1994, Graffham Press Ltd. ("Rickards") was published in January 1994.

Claim No.	Claim Language	Description
		to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-43

"Current treatment of BPH"

("Roylance")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Roylance teaches a method for the prophylaxis and treatment of benign prostatic hyperplasia ("BPH".) (*See, e.g.*, p.334.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Roylance teaches the administration of an effective amount of *Serenoa repens* under the brand name Permixon® for treatment of BPH to a person in need thereof. (*See, e.g.*, p. 334.) The plant extract, saw palmetto extract (also referred to as *Serenoa repens*, has been shown to have PDE V inhibition activity. (*See, e.g.*, Yang, Surong, et al. "Saw Palmetto Extract Enhances Erectile Responses by Inhibition of Phosphodiesterase 5 Activity and Increase in Inducible Nitric Oxide Synthase Messenger Ribonucleic Acid Expression in Rat and Rabbit Corpus Cavernosum." Urology 81.6 (2013): 1380-e7.) Roylance further teaches the administration of an effective amount of the balm of Gilead for treatment of BPH to a person in need thereof. (p. 334.) Roylance also discloses multiple pharmacological choices for the treatment of BPH which also render obvious the claimed invention. For example, Roylance teaches the administration of various alpha-blockers to treat BPH, noting their action on bladder and prostate smooth muscle, the contraction of which is mediated through alpha-receptors. Treatment with the alpha-blockers results in increased uroflow, decreased residual volume, and a decrease in symptoms of BPH. (p. 335.) In addition, Roylance discusses the treatment of BPH with finasteride, a 5alpha-reductase inhibitor approved for the treatment of BPH

[1] P. Roylance, B. Gibelin and J. Espie, "Current treatment of BPH" Biomed & Pharmaother (1995) 49, 332-338. ("Roylance") was published in January 1995.

Claim No.	Claim Language	Description
		which decreases prostate volume and improved BPH symptoms. (pp. 335-337.) Roylance makes clear that both finasteride and alpha antagonists are proven effective medical therapies for the treatment of BPH.
3. (a)	The method of claim 1	Roylance teaches a method for the prophylaxis and treatment of benign prostatic hyperplasia ("BPH".) (*See, e.g.*, p.334.) Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed

Claim No.	Claim Language	Description
		invention of the ‘124 Patent.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The clinical studies reported on by Roylance would include compounds in combination with pharmacologically acceptable excipients administered in unit dose form. Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-44

"A review of flavoxate hydrochloride in the treatment of urge incontinence"

("Ruffman")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Ruffman teaches a method for the prophylaxis or treatment of benign prostatic hyperplasia. (*See, e.g.* pp. 322-328.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Ruffman teaches the administration to a person in need thereof an effective amount of at least two phosphodiesterase inhibitors, Eviprostat (a PDE V inhibitor) and flavoxate hydrochloride, alone or in combination with each other. (*See, e.g.*, p. 317, 323.) Ruffman teaches the use of Eviprostat (*see, e.g.* p. 323) which contains equisetum arvense as shown in Tanaka, Tomoaki, et al. "Suppressive effects of Eviprostat, a phytotherapeutic agent, on lower urinary tract symptoms in prostate cancer patients treated with brachytherapy." LUTS: Lower Urinary Tract Symptoms 4.1 (2012): 25-28 ("Tanaka") at p. 25; equisetum arvense contains several components, including, quercetin, luteolin and kaempferol as shown in Veit, Markus, et al. "Interspecific and intraspecific variation of phenolics in the genus Equisetum subgenus Equisetum." Phytochemistry 38.4 (1995): 881-891 ("Veit") at p. 883 and *generally*; quercetin, luteolin and kaempferol are PDE V inhibitors as shown in Lines, T. C., and M. Ono. "FRS 1000, an extract of red onion peel, strongly inhibits phosphodiesterase 5A (PDE 5A)." Phytomedicine 13.4 (2006): 236-239 ("Lines") at pp. 236, 238, and *generally*, Ko, Wun-Chang, et al. "Inhibitory effects of flavonoids on phosphodiesterase isozymes from guinea pig and their structure–

[1] Ruffmann, R. "A review of flavoxate hydrochloride in the treatment of urge incontinence." Journal of international medical research 16.5 (1988): 317-330. ("Ruffman") was published in October 1988.

Claim No.	Claim Language	Description
		activity relationships." Biochemical pharmacology 68.10 (2004): 2087-2094 ("Ko") at pp. 2087, 2092 and *generally*, and Yu, Ming-Chih, et al. "Luteolin, a non-selective competitive inhibitor of phosphodiesterases 1–5, displaced [3 H]-rolipram from high-affinity rolipram binding sites and reversed xylazine/ketamine-induced anesthesia." European journal of pharmacology 627.1 (2010): 269-275 ("Yu 3") at p. 269 and *generally*.) Ruffman also discloses use of flavoxate extensively in the treatment of urinary tract disorders characterized by smooth muscle spasm. Flavoxate is disclosed as a spasmolytic with potent smooth muscle relaxant properties, which affects the buildup of tension in the bladder wall during the non-cholinergic phase of urine storage, resulting in an increase of bladder compliance. Flavoxate has been shown to exert inhibitory activity on cAMP-dependent phosphodiesterase in various tissues, including the lung, stomach, bladder and ureter and that this PDE inhibition is crucial for smooth muscle relaxation. (pp. 319-320.) Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of

Claim No.	Claim Language	Description
		PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Ruffman teaches the combination of the disclosed compounds with a pharmacologically acceptable excipient administered in a unit dose form. (*See,* pp. 317, 323-328.) Moreover, The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-45

"Efficacy and side-effects of prazosin as a symptomatic treatment of benign prostatic obstruction"

("Ruutu")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Ruutu teaches a method for the prophylaxis and treatment of benign prostatic hyperplasia ("BPH".) (*See, e.g.*, pp.15-17.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	Ruutu teaches the administration of an effective amount of prazosin, an alpha-adrenoreceptor blocking drug, to a person in need thereof. (*See, e.g.*, pp. 15-17.) Prazosin was known to result vasodilation and reduced peripheral resistance in the vascular smooth muscle. Ruutu teaches that the smooth muscle relaxation mechanism of action is not limited to vascular smooth muscle but also applies to other smooth muscle tissue, including the smooth muscle of the lower urinary tract. Ruutu discloses data confirming that alpha-adrenoreceptor blocking drugs improve urinary flow objectively and subjectively by relaxation of prostatic and urethral smooth muscle tissue. (*Id.)* Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the

[1] M. Ruutu et al., "Efficacy and side effects of Prazosin as a symptomatic treatment of benign prostatic obstruction," Scand J Urol Nephrol 25:15-19 (1991). ("Ruutu") was published in January 1991.

Claim No.	Claim Language	Description
		prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-46

"A selective type V phosphodiesterase inhibitor, E4021, dilates porcine large coronary artery"

("Sakei")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Saeki discloses the use of inhibitors of PDE V for treatment of diseases where smooth muscle relaxation is beneficial, such as heart failure, pulmonary hypertension and angina. Saeki does not expressly disclose the treatment of BPH; however, one of ordinary skill in the art would be motivated to use the inhibitors of PDE V, such as E4021, to induce smooth muscle relaxation in order to treat BPH.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-	Saeki reference discloses a selective PDE V inhibitor (E4021) (which compound (d) disclosed in the '124 Patent) for the use in relaxing vascular smooth muscle. Saeki investigated the inhibitory effects of E4021 on five PDE isozymes isolated from porcine aortic smooth muscle and found that E4021 specifically inhibited type V PDE cGMP-specific PDE. Saeki also compared E4021 to Zaprinast. (*See, e.g., Abstract, p. 825)* Saeki states that "[i]ncrease in intracellular is well known to cause vasodilation" and, for example, "nitrates relax vascular smooth muscle through the stimulation of cGMP synthesis, and conversely, inhibitors of cGMP hydrolysis are expected to cause vasodilation." *(See p. 825)* Saeki teaches that selective inhibitors of PDE V, such as E4021, should have therapeutic applications in various diseases where relaxation of the smooth muscle is beneficial. Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it

[1] Saeki, Takao, et al. "A selective type V phosphodiesterase inhibitor, E4021, dilates porcine large coronary artery." Journal of Pharmacology and Experimental Therapeutics 272.2 (1995): 825-831 was accepted for publication on October 10, 1994. ("Saeki") was published in February 1995.

Claim No.	Claim Language	Description
	propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition

Claim No.	Claim Language	Description
		(1995))

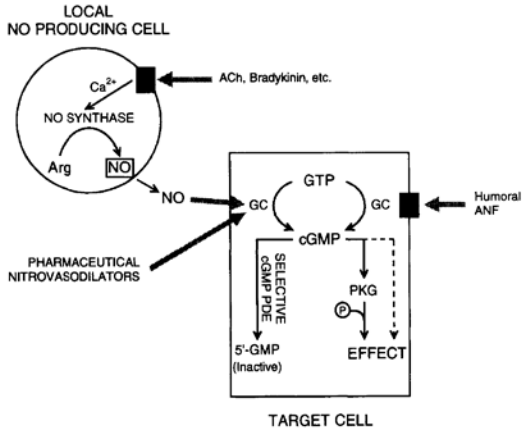
Exhibit A-47

"Phosphodiesterase Inhibitors"

("Schudt")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Schudt discloses the use of various PDE inhibitors, including PDE V inhibitors, for various medical treatment therapies. Schudt expressly teaches that inhibitors of PDE V are beneficial therapeutic agents to achieve or induce relaxation of smooth muscle. Based upon the known smooth muscle relaxant activity of PDE V inhibitors, and the known therapeutic target of smooth muscle relaxation to treat BPH, it would have been obvious to use the PDE V inhibitors disclosed in Schudt for the prophylaxis or treatment of BPH.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one,	Schudt provides a comprehensive overview of PDE inhibitors in general, including two chapters on PDE V inhibitors. (See generally pp. 127-146) Schudt, in the chapter authored by Paul J. Silver, teaches that "the therapeutic rationale for PDE5 inhibitors derives solely from the ability to potentiate or perpetuate the activity of increased cGMP levels brought about by the activation of guanylate cyclase (GC)." (p. 127) Schudt notes that cGMP "has long been recognized as having smooth muscle relaxant activity as well as anti-aggregatory activity in platelets, a logical place for therapeutic intervention involves these two cell types." (p. 127-28) In addition, because PDE V is disclosed to found in most smooth muscles, any tissue having smooth muscle would be logical place of therapeutic intervention to relax that smooth muscle via the cGMP pathway. (p 128) Schudt further discloses the important relationship between NO and cGMP activity, noting that NO increases cGMP in various smooth muscles (airway,

[1] Schudt, C., et al. (1996). Phosphodiesterase Inhibitors, Academic Press. Schudt was published August 27, 1996.

Claim No.	Claim Language	Description
	• 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	vascular and penis). (e.g., pp. 128, 131) Schudt teaches the basis for activity of PDE V inhibition as shown schematically in Figure 8.1 below:  **Figure 8.1 Schematic representation for the activity of cGMP-PDE inhibitors. Cyclic GMP levels are increased in the target cell via activation of soluble guanylate cyclase (GC) by local NO producing cells or exogenous NO donors such as nitrovasodilators. Particulate GC is activated via ANF binding to a receptor. Increased intracellular levels of cGMP produce their effect via activation of cGMP-dependent protein kinase (PKG). Intracellular cGMP is also degraded by cGMP-specific PDE. Inhibition of this PDE potentiates or prolongs the activity of these GC activators.** (p. 128) Schudt discloses several compounds as inhibitors of PDE V, including zaprinast, WIN 58237, IBMX, ORG 30029, (e.g., pp. 128-29, 136-39, 152). Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the

Claim No.	Claim Language	Description
		lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See*, *e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-48

("Serenoa Repens")
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Serenoa Repens (*e.g.*, Saw Palmetto or Permixon) has been used for decades in a method for the prophylaxis and treatment of benign prostatic hyperplasia. (*See, e.g.*, Champault, G., J. C. Patel, and A. M. Bonnard. "A double-blind trial of an extract of the plant Serenoa repens in benign prostatic hyperplasia." British journal of clinical pharmacology 18.3 (1984): 461-462 ("Champault") *generally*, Di Silverio, F., et al. "Plant extracts in BPH." Minerva urologica e nefrologica= The Italian journal of urology and nephrology 45.4 (1993): 143-149 ("Di Silvero") at p. 143 and *generally*, Kim, Sae Woong. "Phytotherapy: emerging therapeutic option in urologic disease." Translational Andrology and Urology 1.3 (2012): 181-191 ("Kim") at p. 182-183, Narayan, Perinchery, and Ramaiah Indudhara. "Pharmacotherapy for benign prostatic hyperplasia." Western journal of medicine 161.5 (1994): 495 ("Narayan") at p. 498, Plosker, Greg L., and Rex N. Brogden. "Serenoa repens (Permixon®)." Drugs & aging 9.5 (1996): 379-395 ("Plosker") at p. 379 and *generally*, Rickards, D. and T. J. Christmas (1994). Benign prostatic hyperplasia: A Colour Guide, Graftham Press ("Rickards"), Roylance, P., B. Gibelin, and J. Espie. "Current treatment of BPH." Biomedicine & pharmacotherapy 49.7 (1995): 332-338 ("Roylance") at p. 334-335, and Yang, Surong, et al. "Saw Palmetto Extract Enhances Erectile Responses by Inhibition of Phosphodiesterase 5 Activity and Increase in Inducible Nitric Oxide Synthase Messenger Ribonucleic Acid Expression in Rat and Rabbit Corpus Cavernosum." Urology 81.6 (2013): 1380-e7 ("Yang") at p. 1380(e7) and *generally*.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound	The method teaches the administration of an effective amount of Serenoa Repens, which include as an active ingredient a PDE V

Claim No.	Claim Language	Description
	selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	inhibitor, to a person in need thereof. (*See, e.g.* Champault, *generally*, Di Silverio at p. 147, Kim at p. 182-183, Plosker at p. 384 and *generally*, and Yang at 1380.e8 and *generally*. Yang also teaches that Serenoa Repens contains at least one compound that is a PDE V inhibitor (*see* Yang, *generally*).) This treatment has been available and used for decades to prevent and treat BPH. Defendants reserve the right to identify additional prior art references which show the extensive use of various herbal extract-based medications which include a PDE V inhibitor and which anticipate and/or render obvious the claimed invention. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references

Claim No.	Claim Language	Description
		provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	Serenoa Repens (e.g., Saw Palmetto) has been used for decades for the method of claim 1; *see* description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Serenoa Repens (e.g., Saw Palmetto) has been used for decades in a method for the prophylaxis and treatment of benign prostatic hyperplasia in combination with a pharmacologically acceptable excipient that is administered in a unit dose form. (*See, e.g.* Champault, *generally*, Di Silverio at p. 147, Plosker at p. 384 and *generally*, and Yang at 1380.e8 and *generally*.) This treatment has been available and used for decades to prevent and treat BPH. Defendants reserve the right to identify additional prior art references which show the extensive use of various herbal extract-based medications which include a PDE V inhibitor and which anticipate and/or render obvious the claimed invention.

Exhibit A-49

"Characterization of Human Platelet Cyclic Nucleotide Phosphodiesterase (PDE) Iso-Enzyme and their Sensitivity to a Variety of Selective Inhibitors"

("Shahid")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Shahid discloses that OG 30029 (N-hydroxy-5, 6-dimethoxybenzo-[b]-thiophene-2-carboximidamide) inhibits PDE5 in fresh human platelets.
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one,	Shahid tests OG 30029 (N-hydroxy-5, 6-dimethoxybenzo-[b]-thiophene-2-carboximidamide). Shahid discloses that the new cardiotonic agent Org 30029 inhibited both cG-spec and cG-inhib PDEs. cG-Spec PDE is, at least inherently, PDE V. Shahid also tests Zaprinast, which is a PDE5 inhibitor. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE

[1] Abstract 443P, M. Shahid, M. Holbrook, S.J. Cokert, and C.D. Nicholson, "Characterization of Human Platelet Cyclic Nucleotide Phosphodiesterase (PDE) Iso-Enzyme and their Sensitivity to a Variety of Selective Inhibitors", published as Shahid, M. & Rodger, I.W. (1989), Br. J. Pharmacol. 98, 291-301. ("Shahid") was published in December 1990.

Claim No.	Claim Language	Description
	and pharmacologically compatible salts thereof.	V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-50

United State Patent No. 5,439,895

("Sung '895")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising administering to a person in need thereof	Sung '895 discloses inhibition of cGMP-PDE with 4-aminoquinazolines. Till now, it has been known that cGMP is distributed broadly in tissues of many animals including human beings. cGMP is biosynthesized from guanosine triphosphate (GTP) by the action of guanylate cyclase. cGMP has been experimentally confirmed to have various physiological activities. For example, cGMP induces the relaxation of heart muscle and of smooth muscle. Further, it is related to the formation of neuronal synapses, and it acts as a trigger of cell proliferation and it induces the proliferation of lymphocyte. cGMP is metabolized to physiologically inactive 5'-GMP by the action of cGMP phosphodiesterase (abbreviated as cGMP-PDE hereafter). Accordingly, the inhibition of the action of cGMP-PDE is considered to be useful for the prevention and/or treatment of diseases induced by enhancement of the metabolism of cGMP… (See column 1, lines 48 through 62.) Sung '895 states that the disclosed compounds are useful for the prevention or treatment of various diseases and symptoms, including renal insufficiency, which is a known effect of BPH. (Col. 16:35-45; see also claim 17)
1. (b)	an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-	Sung '895 discloses aminoquinazoline inhibitors of phosphodiesterase (PDE) V. Sung '895 discloses zaprinast. (Col. 2:55-64). Sung '895 discloses methods of prevention and treatment of humans by administering an effective amount of the

[1] U.S. Patent No. 5,439,895 ("Sung '895") was filed on November 19, 1993 was issued on August 8, 1995, claims a priority date of July 15, 1992, and is titled "4-aminoquinazoline derivatives."

Claim No.	Claim Language	Description
	(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	disclosed quinazoline derivative compounds that inhibit PDE V. (Col. 4:29-5:32) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Sung '895 discloses compounds in combination with pharmacologically acceptable excipients administered in unit

Claim No.	Claim Language	Description
		dose form. (see Col. 18:22-19:47) Sung '895 provides [t]he doses to be administered are determined depending upon age, body weight, symptom, the desired therapeutic effect, the route of administration, and the duration of the treatment etc. In the human adult, the doses per person are generally between 1 mg and 1000 mg, by oral administration, up to several times per day, and between 1 mg and 100 mg, by parenteral administration up to several times per day, or continuous administration between 1 and 24 hrs. per day intravenously. (Col. 18:29-37)

Exhibit A-51

"cGMP phosphodiesterase inhibition: A new mechanism for the discovery of therapeutic agents"

("Sybertz")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Sybertz discloses that PDE V binds cGMP and selectively hydrolyzes cGMP. (p. 384) PDE V is taught to be distributed in several tissues, including lung, kidney, platelets, endothelial cells, and smooth muscle cells and spleen; and that the PDE V enzyme plays a key role in the hydrolysis of cGMP in differing tissues. (p. 373, 384) Sybertz states that "[t]he evolving biology of cGMP and understanding of its mechanisms of regulation are opening up new opportunities for discovery of drugs which can produce therapeutically desirable effects through alteration of cGMP levels." (Abstract)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole,	Sybertz discloses various PDE I and PDE V inhibitors such as Zaprinast, papaverine, IBMX, Sulmazole, Griseolic Acid, and SCH 51866. (e.g., pp. 385-88) Sybertz reports studies by Eisai into quinazoline based PDE V inhibitors, including more than 140 quinazoline structures in two patent applications. (p. 376-78) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the

[1] Sybertz, E. J., M. Czarniecki, and H. S. Ahn. "cGMP phosphodiesterase inhibition: A new mechanism for the discovery of therapeutic agents." Current Pharma. Design 1.4 (1995): 373-390.

Claim No.	Claim Language	Description
	• 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Sybertz discloses the use of a compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form (intravenous administration, for example, at p. 386). Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See*, *e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-52

"Characterization of cyclic nucleotide phosphodiesterase isoenzymes in the human ureter and their functional role in vitro"

("Taher")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Taher discloses the characterization of cycle nucleotide PDE isoenzymes in the human ureter and their functional role in vitro. Taher teaches that cAMP and cGMP play an important role in the regulation of smooth muscle tone. (p. 286)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one,	Taher discloses Zaprinast as an inhibitor of phosphodiesterase (PDE) V and papaverine as a nonselective PDE inhibitor (papaverine is known to inhibit PDE V). (p. 288-89; Table 2) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of

[1] A. Taher, et al., Charaacterization of cyclic nucleotide phosphodiesterase isoenzymes in the human ureter and their functional role in vitro, World J Urol (1994) 12:286-291. ("Taher") was published October 31, 1994.

Claim No.	Claim Language	Description
	and pharmacologically compatible salts thereof.	PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.,* The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-53

Canadian Patent No. 2,197,984 ("Takayama '984")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Takayama '984 discloses a method for prophylaxis or treatment of benign prostatic hyperplasia. Takayama '984 discloses that the compounds of the invention of Takayama '984 are useful as an agent for the prevention or treatment of various diseases, including "diseases related to micturition (e.g., diabetes insipidus, urethritis, urinary incontinence, cystitis, irritable bladder, neurogenic bladder, uremia, tubular disorder, pollakiuria, urinary retention and the like), … prostatic hypertrophy…." (e.g., p. 39)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one,	Takayama '984 discloses administering 1, 8-naphthridine derivatives as inhibitors of phosphodiesterase (PDE) V. (p. 48-49) Table on p. 49 discloses multiple examples of 1, 8 naphthyridine derivatives that inhibit PDE V isolated from peripheral blood.

[1] Canadian Patent No. 2,197,984 ("Takayama '984") was filed on August 28, 1995, was issued on March 7, 1996, claims a priority date of August 29, 1994, and is titled "Novel Naphthyridine Derivatives and Pharmaceutical Compositions Thereof."

Claim No.	Claim Language	Description
	• 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	

Compound	IC_{50} (μM)				
	Type I	Type II	Type III	Type IV	Type V
Example 15	0.0338	20.8	50.3	58.9	41.2
Example 24	0.0419	51.8	21.5	98.3	9.7
Example 26	0.0234	30.0	56.2	84.9	27.3
Example 27	0.0213	25.6	15.5	> 30	27.9
Example 29	0.0116	15.5	14.3	> 30	24.6
Example 30	0.0099	10.5	10.9	31.2	8.66
Example 31	0.0043	> 30	> 30	> 30	> 30
Example 33	0.0143	35.4	17.7	> 30	8.39
Example 35	0.0242	22.3	34.4	21.9	41.6
Example 38	0.0124	26.1	> 30	> 30	19.6
Example 39	0.0025	> 3	> 3	> 3	1.05
Example 40	0.0129	20.5	32.3	31.9	14.5
Example 43	0.0160	> 30	> 30	> 30	4.79
Example 46	0.0389	> 30	> 30	> 30	87.0
Example 49	0.0337	22.8	27.3	30.2	3.87
Comparative Compound A	0.250	> 30	> 30	> 30	31.5

Comparative compound A: Example 1 in International Publication 94/12499

[*Note: Per the certificate of correction filed in the U.S. counterpart, U.S. patent no. 5,817,670, the above Table was corrected to reflect that column headings should read Compound, Type IV, Type I, Type II, Type III, Type V).*

Thus, examples of the disclosed compound (at least, Example 39, Example 49) demonstrate potent inhibition of PDE V.

Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known

Claim No.	Claim Language	Description
		methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Takayama '984 discloses that compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form. "A pharmaceutical preparation which contains one or a plurality of the compounds of the present invention or salts thereof as the active ingredient is prepared using carriers, excipients and other additive agents generally used in the preparation of pharmaceuticals …. It [the compound] can be administered by oral administration in the dosage form of tablets, pills, capsules, granules, powders, solutions and the like or by parenteral administration in the form of injections (e.g., intravenous, intramuscular and the like), suppositories, transdermal preparations, inhalants and the like or by intravesical

Claim No.	Claim Language	Description
		injection. The dose is optionally decided case by case taking symptoms, age, sex and the like of each patient into consideration, and it may be generally from about 0.001 mg/kg to about 100 mg/kg per day per adult in the case of oral administration, and the daily dose may be used once a day or divided into 2 to 4 doses per day. (pp. 51-52; see also pp. 53-54). Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995)).

Exhibit A-54

"Effects of nitric oxide on human and canine prostates"

("Takeda")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Takeda discloses a method for prophylaxis or treatment of benign prostatic hyperplasia symptoms by relaxing the prostate smooth muscles. "The development of bladder outlet obstruction in men with benign prostatic hyperplasia (BPH) has been shown to be related to the area density of prostate smooth muscle." (p. 441) Takeda further discloses that mediation of prostatic smooth muscle tension (i.e., relaxation) can "improve urinary flow rates and urinary symptoms in men with BPH" and that mediators of prostatic smooth muscle activity have important implications in the treatment of BPH. (p. 441).
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-	Takeda discloses relaxation of the prostatic smooth muscles using alpha blockers. "Several randomized double-blind placebo-controlled studies have provided indisputable evidence that alpha blockers significantly improve the symptomology and urinary flow rates in men with BPH. It is, therefore, reasonable to speculate that pharmacologic manipulation of other endogenous mediators of prostatic smooth muscle tension may have a therapeutic application in the treatment of BPH." (p. 444) Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in

[1] Takeda, Masayuki, et al. "Effects of nitric oxide on human and canine prostates." Urology 45.3 (1995): 440-446. ("Takeda") was published in March 1995.

Claim No.	Claim Language	Description
	d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	The use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-55

German Patent Application Publication 195 40 642

("Truss '642")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Truss '642 discloses a method for prophylaxis or treatment of benign prostatic hyperplasia comprising use of various PDE inhibitors. The subject matter of the invention is therefore the use of specific inhibitors of sPDE I, sPDE IV and sPDE V for prophylactic treatment and for the treatment of diseases of the prostate, in particular benign prostatic hyperplasia. (Col: 2:19-23)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-	Truss '642 discloses various inhibitors of phosphodiesterase (PDE) V, including at lease one inhibitor of PDE V (ORG 30029 (N-hydroxy-5, 6-dimethoxybenzo-[b]-thiophene-2-carboximidamide)) disclosed in the '124 Patent or included in the claimed exclusion group. (Col. 2:31-60) Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention.

[1] German Patent Application Publication 195 40 642 ("Truss '642") was filed on November 1, 1995, was published on May 7, 1997, claims a priority date of November 1, 1997, and is titled "Use of phosphodiesterase I, IV and V inhibitors."

Claim No.	Claim Language	Description
	propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Truss '642 discloses: "Suitable administration forms are oral, intravenous, transdermal, subcutaneous and intravesical preparations. The latter are particularly solutions and preparations such as are used for parenteral administration. Preparations for parenteral administration contain 0.15 μg to 1 mg, preferably 5 to 500 μg of the compounds of general formula II per dosage unit and can be provided in separate dosage unit forms, such as, e.g., ampoules or vials." (Col. 3:24-31)

Exhibit A-56

Japanese Unexamined Patent Application Disclosure No. H7 188214

("Yoshitaka '214")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Yoshitaka '214 discloses a method of treating various diseases via the cGMP pathway involving the relaxation of smooth muscles. Yoshitaka does not explicitly disclose benign prostatic hyperplasia, but one of ordinary skill in the art would be motivated to use disclosed inhibitors of cGMP-specific PDEs (including PDE V) known to induce smooth muscle relaxation in order to treat BPH, including known symptoms secondary to BPH, such as renal diseases including renal failure. (pp. 3, 11)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one,	Yoshitaka '214 discloses treating a patient having a disease which would benefit from the inducement of smooth muscle relaxation, including renal diseases and renal failure, by administering an inhibitor of cGMP-specific PDEs (including PDE V) to a patient in need of such treatment. (pp. 2-3, 11) Based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the

[1] Japanese Unexamined Patent Application Disclosure No. H7 188214 ("Yoshitaka '214") was December 24, 1993, published on July 25, 1995, and is titled "4-aminoquinazoline derivative, method for producing same, and pharmaceutical agent containing same."

Claim No.	Claim Language	Description
	• 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Yoshitaka '214 discloses the dosages used and various methods of administration of the dosage, with a preferred administration and dosage level. pp. 11-12. Moreover, the use of the disclosed compound in combination with a pharmacologically acceptable excipient administered in a unit dose form would be obvious to, and within the routine, conventional knowledge and experience, of a person of ordinary skill in the art. (*See, e.g.*, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 12th edition (1996); Remington: The Science and Practice of Pharmacy, 19th edition (1995))

Exhibit A-57

"TCM Management: Benign Prostate Hyperplasia (Long Bi - Prostatism)"

("Cheung")[1]
vs.
Claims of the '124 Patent

Claim No.	Claim Language	Description
1. (a)	A method for prophylaxis or treatment of benign prostatic hyperplasia comprising	Epimedium herbs (*e.g.*, Horny Goat Weed) have been used for centuries in a method for the prophylaxis and treatment of benign prostatic hyperplasia. (*See, e.g.*, Flaws, Bob, et al. "The treatment of modern Western medical diseases with Chinese medicine: a textbook & clinical manual." Blue Poppy Enterprises, Inc., 2001 ("Flaws") at pp. 91, 93, and 94.)
1. (b)	administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of • dipyridamole, • 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline, • 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate. • 4((3,4-(methylendioxy)benzyl 1)amino)-6,7,8-trimethoxy-quinazoline, • 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole [4,5]pyrimidin-4(5H)one, • 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole, • 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one, • 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chro nan-4-one,	The method teaches the administration of an effective amount of epimedium herbs, which include as an active ingredient a PDE V inhibitor, to a person in need thereof. (*See, e.g.* the formulae taught in Flaws at pp. 91, 93, and 94; the administration of Horny Goat Weed (Epimedium Herbs) for more than 2000 years as taught in Kim, Sae Woong. "Phytotherapy: emerging therapeutic option in urologic disease." Translational Andrology and Urology 1.3 (2012): 181-191 ("Kim") at pp. 185-186; Kim also teaches that icariin, the active compound in epimedium herbs is a PDE V inhibitor (see Kim at pp. 185-186); this is also taught in Ma, Huiping, et al. "The genus Epimedium: an ethnopharmacological and phytochemical review." Journal of ethnopharmacology 134.3 (2011): 519-541 ("Ma") at p. 531 and *generally*, in Ning, Hongxiu, et al. "Effects of icariin on phosphodiesterase-5 activity in vitro and cyclic guanosine monophosphate level in cavernous smooth muscle cells." Urology 68.6 (2006): 1350-1354 ("Ning") at p. 1351 and *generally*, and in Xin, Z. C., et al. "Effects of icariin on cGMP-specific PDE5 and cAMP-specific PDE4

[1] Cheung, C.S. and Deaton, K., TCM Management: Benign Prostate Hyperplasia (Long Bi - Prostatism), Harmonious Sunshine Cultural Center, 1994. ("Cheung") was published in 1994.

Claim No.	Claim Language	Description
	• 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, and pharmacologically compatible salts thereof.	activities." Asian journal of andrology 5.1 (2003): 15-18 ("Xin"), *generally*. Horny Goat Weed (Epimedium Herbs) also contains quercetin, luteolin, naringenin, luteolin and kaempferol, which are also PDE V inhibitors as shown in Ma at p. 531 and *generally*, Lines, T. C., and M. Ono. "FRS 1000, an extract of red onion peel, strongly inhibits phosphodiesterase 5A (PDE 5A)." Phytomedicine 13.4 (2006): 236-239 ("Lines") at pp. 236, 238, and *generally*, Ko, Wun-Chang, et al. "Inhibitory effects of flavonoids on phosphodiesterase isozymes from guinea pig and their structure–activity relationships." Biochemical pharmacology 68.10 (2004): 2087-2094 ("Ko") at pp. 2087, 2092 and *generally*, Orallo, Francisco, et al. "Implication of cyclic nucleotide phosphodiesterase inhibition in the vasorelaxant activity of the citrus-fruits flavonoid (+/-)-naringenin." Planta medica 71.2 (2005): 99-107 ("Orallo") at p. 99 and *generally*, and Yu, Ming-Chih, et al. "Luteolin, a non-selective competitive inhibitor of phosphodiesterases 1–5, displaced [3 H]-rolipram from high-affinity rolipram binding sites and reversed xylazine/ketamine-induced anesthesia." European journal of pharmacology 627.1 (2010): 269-275 ("Yu 3") at p. 269 and *generally*.) This treatment has been available and used for centuries to prevent and treat BPH. Due to translation issues, Defendants reserve the right to identify additional prior art references which show the extensive use of epimedium herbs which include a PDE V inhibitor and which anticipate and/or render obvious the claimed invention. Moreover, based upon the teachings of this reference, other references provided herewith, and application of ordinary skill in the art, it would have been obvious to a person of ordinary skill in the art to administer an effective amount of an inhibitor of PDE V to a person in need of prophylaxis or treatment of BPH. The

Claim No.	Claim Language	Description
		claimed elements were known in the prior art, and one skilled in the art could have combined the claimed elements using known methods to yield reasonably predictable results. The relaxation of the lower urinary tract smooth muscle, including that of the prostate, was a known and recognized therapeutic target for the prophylaxis or treatment of BPH at the time of the invention. There were a finite number of ways known at the time of the invention to relax lower urinary tract smooth muscle, including that of the prostate. The mechanism of action of inhibitors of PDE V to relax smooth muscle was known and recognized at the time of the invention. It would have been obvious to try inhibitors of PDE V to achieve a reasonably predictable result of relaxation of lower urinary tract smooth muscle, including that of the prostate, with a reasonable expectation of success for the prophylaxis or treatment of BPH. A person of ordinary skill in the art would have been motivated by that person's own knowledge, the teachings and suggestions in this reference and other references provided herewith, and market forces (such as the need for medical, non-invasive and less expensive treatments for condition affecting a large portion of the male population), to combine and use the known mechanism of action of PDE V inhibitors to induce known and reasonably predictable therapeutic objectives for the prophylaxis or treatment of BPH to arrive at the claimed invention of the '124 Patent.
3. (a)	The method of claim 1	See description for claim 1 above.
3. (b)	wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.	Epimedium herbs (*e.g.*, Horny Goat Weed) have been used for centuries in a method for the prophylaxis and treatment of benign prostatic hyperplasia in combination with a pharmacologically acceptable excipient that is administered in a unit dose form. (*See, e.g.* the formulae taught in Flaws at pp. 91, 93, and 94.) This treatment has been available and used for centuries to prevent and treat BPH. Due to translation issues, Defendants reserve the right to identify additional prior art references which show the extensive use of epimedium herbs which include a PDE

Claim No.	Claim Language	Description
		V inhibitor and which anticipate and/or render obvious the claimed invention.